The management of insomnia: an update

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SYNOPSIS

Insomnia is a common symptom but hypnotics should be avoided if possible. Management aims to identify and treat underlying causes, such as psychiatric disorders and medical problems. If symptomatic relief is still required in addition to medical, psychological and social interventions, hypnotics can be considered. Hypnotics should preferably be used intermittently, for less than two to four weeks. The newer non-benzodiazepine hypnotics – zopiclone, zolpidem and zaleplon – are not free of the problems surrounding the use of benzodiazepines.

Index words: benzodiazepines, hypnotics.

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Introduction

Insomnia is a common symptom with up to 25% of Australians reporting trouble getting enough sleep.[1] There are many causes for this perceived inadequacy of sleep, but subjective perceptions do not necessarily mean the patient is not sleeping.

Underlying causes of insomnia

Symptoms associated with insomnia may suggest an underlying medical, surgical, psychological or environmental problem. Treating any underlying problem can help to alleviate the insomnia.

Psychiatric factors

Psychiatric disorders are typically associated with insomnia. Anxiety disorders can cause early insomnia (difficulty in getting to sleep) associated with rumination over particular worries or concerns. With depression, it is typical to have middle insomnia (waking in the early hours of the morning) and late insomnia (waking earlier in the morning than is usual and being unable to get back to sleep). The depressive pattern may also have an associated anxiety disorder so the patient's sleep is disturbed throughout the night. Patients may present with insomnia and only acknowledge their low mood or loss of interest after enquiry.

Middle insomnia is typical with alcohol abuse. The patient goes to sleep in the evening when intoxicated only to wake a few hours later when their blood alcohol concentration drops.

Environmental factors

If a patient's bedroom is too hot, too cold, too noisy, or their bed cramped or uncomfortable, addressing those factors may resolve the problem. A crying baby, or a sick or restless child or other family member may disturb sleep. The assistance of a partner, other relative, or brief period of respite may address the sleeplessness.

Physical factors

Many illnesses including cardiac and respiratory failure and pain syndromes may contribute to insomnia.

Jet lag

Flying across several time zones may also result in insomnia. The therapeutic key is to settle into the new time zone as quickly as possible. This is aided by a regular local sleep-wake cycle and particularly by re-setting sleep rhythms with early morning light and exercise. It is possible to adjust approximately one hour per day, a task which is easier when the sleep cycle is extended rather than shortened. This is quicker following east to west travel than west to east. A similar disturbance may occur when shift workers start and end work cycles. Occasionally, the brief use of a hypnotic may help adaptation to a new sleep pattern. Taking a hypnotic during flight should generally be avoided as immobility may predispose to deep vein thrombosis.

Evaluation

In addition to routine clinical evaluation, it is worth asking in detail about the patient's sleep pattern (see Box 1). Asking the patient to complete a sleep log over a few days is also useful. The log should be completed as each day progresses, as retrospective entries tend to minimise sleep and maximise disturbances. Patients may enter factors you had not considered, but which may be relevant to the sleep disturbance (Fig. 1).

Box 1

Evaluating a patient's sleep

Determine:

- habits and patterns of getting ready to go to bed
- time of going to bed
- time of going to sleep
- time(s) of waking(s)
- time(s) to get back to sleep
- what the patient does when awake in the night
- features (if any) that help the patient settle
- features that tend to add to the patient's disturbance
- any daytime sleeping, times and duration.

A sleep log will usually help this assessment (Fig. 1).

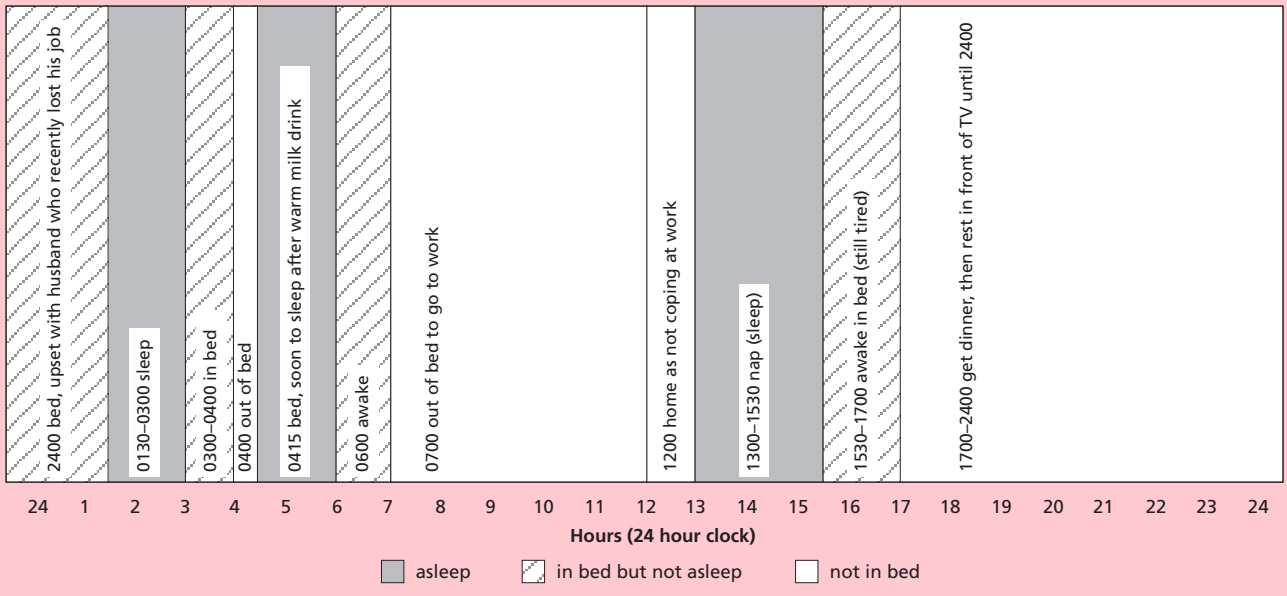
Fig. 1

Sleep log

The patient enters times of going to sleep and when awake, including any daytime naps or sleeps, and any factors that tend to make sleep better or worse, e.g. meals, alcohol. They should also enter the names and times of any medicines taken.

This sleep log helps to establish whether they have early, middle or late insomnia.

Copies of this chart for patient use are available with the electronic version of this article on the *Australian Prescriber* web site www.australianprescriber.com



Sleep hygiene

Sleep hygiene includes a number of social and behavioural interventions to help patients improve their sleep (see Box 2). Cognitive behaviour therapy techniques can also assist some patients.[2,3,4]

Drug treatment of insomnia

General considerations

The prescription of hypnotics should only follow a careful evaluation and consideration of other approaches including psychological interventions such as cognitive behaviour therapy. In general hypnotics should only be prescribed if the duration of use is likely to be less than four weeks, and preferably less than one or two weeks.

Key elements when prescribing are to manage patient expectations of the duration of treatment and likely outcomes, and to have an 'exit' strategy. Explain the likely duration of therapy, when medicines should be used and when they should not be used, common adverse events, and the risks of tolerance, dependency, withdrawal and discontinuation syndromes if use is prolonged.

The exit strategy is a clear plan of change for the patient so that they should not need continued drug treatment. For example, you might expect an antidepressant to have started to work in two to four weeks so that depression-related insomnia should have resolved by that time. Most patients do not need a hypnotic for depression-related insomnia. A few value initial help with sleep, but hypnotics should not be continued once the depression is relieved. Some personal and social crises can

Box 2

Improving your sleep

- Develop a regular pattern of going to bed at about the same time each night, and getting up at about the same time each morning.
- The bedroom should be comfortable and quiet and not the focus of arguments, anger or distress. Avoid clock-watching.
- Substances on which the patient may be dependent, or which cause intoxication or discontinuation syndromes, should be avoided for several hours before bedtime, e.g. caffeine.
- Vigorous exercise, hard work, or activities requiring considerable concentration and arousal should stop some time before going to bed.
- If not sleeping, the patient should either relax in bed and not think about sleep, or get up and stay in a dimly lit room until ready to settle to sleep again.
- Daytime sleeping or naps tend to disrupt night-time sleeping so that although the total hours of sleep are preserved, the patient does not wake refreshed because they have less sleep at night.
- Regardless of the underlying cause, patients may become worried and anxious that the forthcoming night may be disrupted, rather than enjoyed as refreshing sleep. Anxiety management and relaxation techniques may assist in controlling their concerns.

Table 1

Pharmacokinetics of common hypnotics*

Hypnotic	*Time to maximum concentration (hours)*	*Half-life (hours)*
Flunitrazepam	1–2	20–30
Nitrazepam	2 (0.5–5.0)	27 (16–48)
Temazepam capsules (authority PBS)	0.5–1	10 (5–15)
Temazepam tablets (general PBS)	0.5–2	10 (5–15)
Triazolam	1.5±0.7	initial phase 3.4±0.9 terminal phase 7.8±1.5
Zaleplon	1	1
Zolpidem	0.5–3.0	2.4±0.2
Zopiclone	1.75	5.26±0.76

* There is substantial inter-individual variation in the pharmacokinetics of these drugs.

result in the patient becoming so distressed and dysfunctional with insomnia that a few nights assisted sleep helps them reintegrate. They could then be expected to cope with the stresses in their life without the need for ongoing drug treatment. Bereavement would not normally necessitate hypnotics, although they can sometimes be briefly helpful when the bereaved patient is not coping with insomnia.

The hypnotics predominantly used in Australia are benzodiazepines, or non-benzodiazepines acting through benzodiazepine receptors. Other classes of drugs are also used, but are potentially more toxic and would rarely seem to offer any advantage over a benzodiazepine or related drug.

Benzodiazepines

These drugs all have similar actions including sedative-hypnotic, anxiolytic, anticonvulsant, muscle relaxing, and amnesic effects. Although some of the drugs are marketed for different indications, their major differences in practice are brought about by differences in pharmacokinetics.

Half-life (Table 1)

Drugs with longer half-lives may cause appreciable impairment in the morning (on waking). A single dose of temazepam or oxazepam can have actions well into the next day, and nitrazepam and flunitrazepam even more so. There has been a recent campaign to use temazepam tablets rather than capsules (because of the risk of people injecting the contents), however the onset of action and time to maximum effect of temazepam tablets can be slower than one would wish in a hypnotic.

Adverse effects of benzodiazepines

Adverse effects can be anticipated from the normal actions of hypnotics. Excessive or daytime sedation may occur, particularly with drugs that have a longer half-life. The sedative and muscle relaxing activity may combine to increase the risk of ataxia or falls, particularly in the elderly.

The anxiolytic action can be helpful in relieving distress when settling to sleep. However, this can be disadvantageous if it inhibits alertness and responsiveness the following morning.

The anticonvulsant action can result in withdrawal fits if the benzodiazepine is withdrawn abruptly. This risk may increase if a benzodiazepine or related drug is substituted by a sedative antipsychotic or tricyclic antidepressant which is pro-convulsant.

Amnesic effects can result in patients forgetting events soon after taking a dose. They may take extra doses if they forget they have already taken their medication. Some may 'forget' previous cautions about concurrent use of alcohol and anterograde amnesia has been associated with such combined use. Disinhibited behaviour may follow ingestion and hallucinations have been reported, especially at higher doses. Hypnotics, particularly those with a long half-life, can cause cognitive problems the following day.

Newer hypnotics

Zaleplon, zopiclone and zolpidem, although structurally not benzodiazepines, act on the same receptor. While there is a suggestion from animal studies that the new drugs have a more specific hypnotic action, this has not yet been shown in humans. The new drugs are not free of the adverse effects of benzodiazepines and are not necessarily safer medicines. On the contrary, one study suggested that elderly patients taking zolpidem had almost double the risk of hip fracture compared with no medication (adjusted odds ratio 1.95, CI* 1.09–3.51). This risk is greater than that seen with benzodiazepines (1.46, CI 1.21–1.76), antipsychotic medications (1.61, CI 1.29–2.01) and antidepressants (1.46, CI 1.22–1.75).[5]

Zopiclone has a bitter taste as its commonest adverse effect. Zolpidem causes hallucinations in a small proportion of patients, and it should be stopped if these occur. Zaleplon has a short half-life making it useful for sleep-onset insomnia. It may be used during the night if a patient cannot fall asleep as it has less risk of morning sedation. Interestingly, within-night discontinuation effects have not been reported, though one might otherwise expect them given its rapid onset and offset.

Other drugs used as hypnotics

Several other types of drugs are sometimes used as hypnotics, but in general their use is limited by toxicity. These drugs are primarily used for other indications, but as drowsiness is one of their adverse effects they are sometimes prescribed for insomnia.

Sedative antihistamines have prominent anticholinergic effects which can result in confusion, especially in children or the elderly, and should have little or no place in the management of insomnia. They may be effective hypnotics in the short term, but many patients rapidly develop tolerance.

Antidepressants should not be used for insomnia unless the patient also has depression. Tricyclic antidepressants have sedative antihistaminic effects, even at low doses which are sub-therapeutic for depression. They have significant anticholinergic effects leading to confusion, alpha adrenergic blocking effects that can result in marked postural hypotension, and quinidine-like effects with the potential for atrioventricular

* CI confidence interval

block and prolongation of the QT_c interval. Tolerance develops to the sedative effects of tricyclic antidepressants and their potential toxicity generally outweighs their benefit as hypnotics, especially in overdose.

Antipsychotic drugs have been little studied as hypnotics. The toxicity of typical antipsychotics limits their use as hypnotics, while atypical antipsychotics are not suitable and they are only approved for use in schizophrenia.

Stopping long-term hypnotic treatment

By establishing a clear expectation of short-term use when starting treatment with a hypnotic you are more likely to avoid your patient falling into the trap of long-term dependency. If the insomnia persists, it is particularly difficult to stop treatment as the patient fears that stopping the hypnotic will make their insomnia worse.

If it is difficult to stop treatment it is worth reviewing the patient's history, and the possibility of underlying disorders, or dependency on the hypnotic. Reinforcement of sleep hygiene techniques, a gradual process of dose reduction, and intermittent use, with the availability of the hypnotic as 'rescue medication' when needed, may assist the patient in reducing their hypnotic use. Long-term use is particularly an issue for patients who were prescribed hypnotics before problems with this use were recognised. Even if one attempt at discontinuing is unsuccessful, review this regularly as an approach at a different time may have more success. Furthermore, if the patient is actively involved in the process, they can choose a night when they would feel more comfortable about reducing the dose and avoid challenging themselves on a night when they fear sleep will elude them.

There is the occasional patient who does not increase their hypnotic dose, or frequency of use, and remains well on a stable dose, but becomes profoundly dysfunctional if it is ceased. When reviewing such a patient consider dose reduction, or stopping the medicine, as well as the possibility of other illnesses or problems perpetuating the patient's seeming need for a hypnotic.

Summary

Patients should not be given hypnotics when other interventions would be more appropriate. Always address underlying disorders and attend to the patient's sleep hygiene before considering prescribing. Before any hypnotic is prescribed, it is important for the patient to have a clear understanding of the expected outcome and that continued use will be unnecessary. With patients on long-term treatment the aim is to cease hypnotics, not change to a newer drug.

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FURTHER READING

National Prescribing Service patient education material 'Getting a good night's sleep'. http://www.nps.org.au (Go to Topics, Benzodiazepines, Patient education material 'A reduction plan for sleeping tablets and sedatives' page 2)

Professor Tiller has conducted sponsored studies or been a consultant to manufacturers of antidepressants, benzodiazepines, antipsychotics and non-benzodiazepine hypnotics.

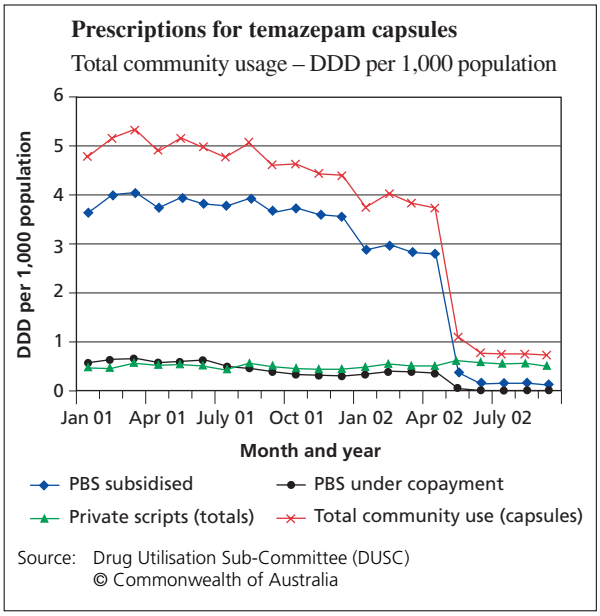
Self-test questions

The following statements are either true or false (answers on page 95)

1. Nitrazepam has a fast onset of action because of its short half-life.
2. Zolpidem may cause more falls in the elderly than benzodiazepines do.

The fall of temazepam capsules

Injecting the contents of a temazepam capsule can cause serious harm. To limit the potential for harm temazepam capsules required an authority prescription from 1 May 2002. This had an immediate effect on the defined daily dose (DDD) per 1000 people.* Although private prescriptions are relatively unchanged, Pharmaceutical Benefits Scheme (PBS) prescriptions have significantly decreased.



* See Birkett D. Monitoring drug use in Australia (Aust Prescr 1993;16:27–9)