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Assessment and management of insomnia

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Insomnia has a major impact on human health, performance, economic productivity and quality of life.^{1,2} Insomnia chronic or severe enough to merit treatment occurs in 8–14% of the general population.³ There are few specialised sleep clinics in Great Britain other than respiratory ones (eg for obstructive sleep apnoea syndrome (OSAS)), most clinicians do not have easy access to psychological treatments, and very often the simplest course of action is the prescription of hypnotic drugs. However, the appropriate use of hypnotics requires an accurate diagnosis of the sleep disorder and knowledge of the pharmacokinetics and dynamics of the available drugs.

The length of total sleep in a day varies in normal adults, with an average of 7–8 hours in the 20–45 year age group. Sleep time and sleep continuity are decreased in older people and increased

daytime napping often leads to a further reduction in the night-time sleep. A normal subject has several short awakenings during the night, most of which are not perceived as awakenings unless they last more than about two minutes. There will probably not be clear consciousness, but subjects may have occasional brief thoughts of how comfortable they feel or how pleased they are that it is not yet time to get up, with an immediate return to sleep. If during the short period of waking some factor causes anxiety or anger (eg aircraft noise, partner's snores or dread of being awake), progress to full awakening and remembering this awakening in the morning are much more likely. The more often this happens, the more subjects complain of unrefreshing sleep. Perhaps the most common cause of irritation derives from 'clock watching': subjects check the time on awakening, remember it and repeat this cycle many times during the night, neglecting periods of sleep in between. This produces anger and frustration, which in turn delay return to sleep and may promote subsequent awakenings.

Diagnosing insomnia

Insomnia is the complaint of poor sleep, with a patient reporting that the duration or subjective quality of sleep is unsatisfactory. It is often accompanied by daytime fatigue, but not usually by daytime sleepiness – it seems that the factors that keep people awake at night also serve to keep them awake in the day. To aid diagnosis of sleep disorders it is

Key Points

Insomnia is the subjective experience of poor or unrefreshing sleep

Insomnia has many factors that should be sought out and treated

Early intervention in acute insomnia may help reduce the likelihood of developing chronic insomnia

'Z' drugs have the highest ratio of efficacy to side effects and are the first-line drug treatment

Hypnotics can be used in certain cases of chronic insomnia if the patient makes an informed choice about the risks of dependence versus the benefits of continued use

KEY WORDS: cognitive behavioural therapy, hypnotics, insomnia, Z drugs

Table 1. Some questions which may be useful in a patient who is complaining about insomnia.

Describing insomnia	<ul style="list-style-type: none"> • What time do you go to bed? Get up? How long does it take you to go off to sleep? • Do you wake up a lot during the night? Does it take you a long time to get back to sleep? • How many 'bad' nights do you have in a week? How does it impact on your daytime activities?
Probing other causes	<ul style="list-style-type: none"> • How has your mood been recently? Do you manage to enjoy your social/family activities? (depression) • Do you find you can't keep still at night? Do your legs twitch in bed? (RLS, PLMS) • Have you been told that you act strangely during your sleep? (parasomnias) • Do you fall asleep suddenly during the day? Do you sometimes go weak when you're emotionally roused, for instance when you're laughing? (narcolepsy) • Have you been told that you snore loudly? Or stop breathing at night? (OSAS)

OSAS = obstructive sleep apnoea syndrome; PLMS = periodic leg movements in sleep; RLS = restless leg syndrome.

important for patients to keep a diary of when they slept and how they felt about their sleep. Some questions to ask patients to help determine the nature and type of their insomnia are shown in Table 1.

It is important to exclude other sleep disorders as a cause of insomnia, particularly restless legs syndrome, usually associated with periodic leg movements in sleep, and parasomnias such as night terrors and sleepwalking. Referral to a specialist sleep centre for objective recording of sleep may be necessary if the presentation is unusual or diagnosis is in doubt, and actigraphy (Fig 1) or polysomnography may be used.

Some precipitating factors in insomnia are listed in Table 2. Timely treatment of short-term insomnia is valuable as it may prevent progression to a chronic condition which is much harder to alleviate. Psychological treatments are effective,⁴ while pharmacotherapy may be either unnecessary or used as a short-term adjunct. The approaches of treatment are to:

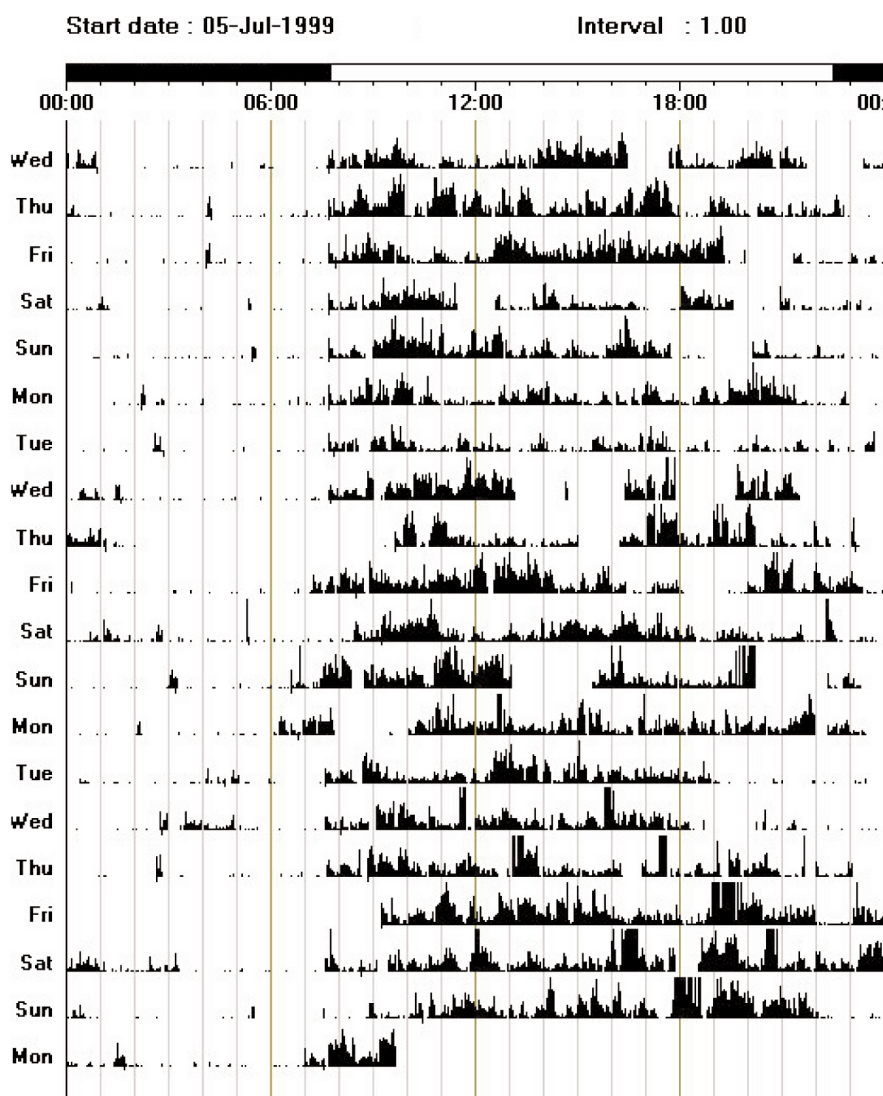
- treat any precipitating cause if possible
- establish good sleep habits (Table 3)
- reassure that sleep will improve
- consider hypnotic medication.

Long-term insomnia

There are various reasons why insomnia can progress to become a long-term problem. The most common are:

- poor sleep hygiene has been established and continues
- the patient has become excessively anxious about their sleep, spending much time and effort on 'trying' to sleep.

◀ **Fig 1. Actigraphy, an objective measure of daily movement over weeks.** Each horizontal line represents a 24-hour period and the height of each vertical bar represents the amount of movement in 1 minute. This insomniac subject adhered to regular rising times and other sleep hygiene measures for the first 8 days, then slipped back into a less regulated regime.



Care should be taken to identify and treat depressive and anxiety disorders in this group of patients.

The most important factor in the treatment of long-term insomnia is anxiety about sleep, arising from conditioning behaviours that predispose to heightened arousal and tension at bedtime. Thus the bedroom is associated with not sleeping and automatic negative thoughts about the sleeping process occur in the evening.

Cognitive behavioural therapy

A helpful treatment approach to anxiety about sleep is cognitive behavioural therapy which, together with education and sleep hygiene measures as above, is the treatment of choice for long-term primary insomnia.⁵ However, the availability of these therapies is often limited and some patients are unwilling or unable to engage with them.

Drugs for insomnia

Most drugs used in insomnia act as agonists at the gamma-aminobutyric acid (GABA)-A-benzodiazepine receptor and have effects other than their direct sedating action, including muscle relaxation, memory impairment and ataxia, which can impair performance of skills such as driving. Those drugs with longer duration of action are likely to affect psychomotor performance, memory and concentration, and will also have enduring anxiolytic and muscle-relaxing effects.

Hypnotics acting at the benzodiazepine receptor

All benzodiazepines and newer benzodiazepine-like ('Z') drugs are safe and effective for insomnia – if the compound with the right timing of onset of action and elimination is chosen. Care should be taken in prescribing them to patients with comorbid sleep-related breathing disorders such as obstructive sleep apnoea syndrome which is exacerbated by benzodiazepines. It is important to stress that alcohol potentiates the effects of these drugs: patients should be made

Table 2. Some precipitating factors in insomnia.

Psychological	Hyperarousal due to:	<ul style="list-style-type: none"> • stress • the need to be vigilant at night because of sick relatives or young children • being 'on-call'
Pharmacological	Prescribed drugs	<ul style="list-style-type: none"> • certain antidepressants, especially SSRIs in first 2 weeks
	Non-prescribed drugs	<ul style="list-style-type: none"> • first 2–3 nights after withdrawal of hypnotics • beta-blockers, beta-agonists sometimes • caffeine • alcohol • cocaine, amphetamine, other stimulants
Physical		<ul style="list-style-type: none"> • pain • pregnancy • coughing or wheezing • respiratory and cardiovascular disorders • need to urinate • neurological disorders (eg stroke) • movement disorders • periodic leg movements of sleep
Psychiatric disorders		<ul style="list-style-type: none"> • depression • anxiety disorder • dementia • substance misuse and withdrawal
Disruption of circadian rhythm		<ul style="list-style-type: none"> • jet lag • shift work

SSRI = selective serotonin reuptake inhibitor.

aware that if they have a drink in the evening, their sleeping pill will have greater and longer-lasting effects which may have an impact on driving the next day. The choice of drug should be determined by pharmacokinetic properties.

A variety of benzodiazepines to treat insomnia is available in UK. The shortest-acting are temazepam, lopro-

zolam and lormetazepam, with half-lives of up to 12 hours. Zopiclone has a half-life of 6–8 hours, making it an effective drug both for initial and maintenance insomnia. Zolpidem and zaleplon have a fast onset (30–60 min) and short durations of action, with half-lives of three hours and two hours, respectively (Fig 2).

Studies of psychomotor performance in volunteers have shown that zaleplon has no effect on psychomotor skills, including driving skills, when taken at least five hours before testing. Thus, it can be taken during the night, either when patients have tried getting off to sleep for a long time or if they wake during the night and cannot return to sleep, without hangover effect. It is the only prescribable hypnotic that can be used in this way.

Hypnotics: tolerance and dependence

Many studies of subjective sleep quality show enduring efficacy of hypnotic drugs but about half of the objective (EEG)

Table 3. Good sleep habits.

- Keep regular bedtimes and rising times
- Reduce daytime napping
- Daytime (but not evening) exercise and exposure to daylight (especially morning sun) are beneficial
- Avoid stimulants, alcohol and cigarettes in evening
- Establish bedtime routine ('wind down'), use some time in early part of evening to write down any residual issues from the current day as well as plans for the coming one
- Avoid dwelling on problems in bed
- Bed should be comfortable and not too warm or too cold

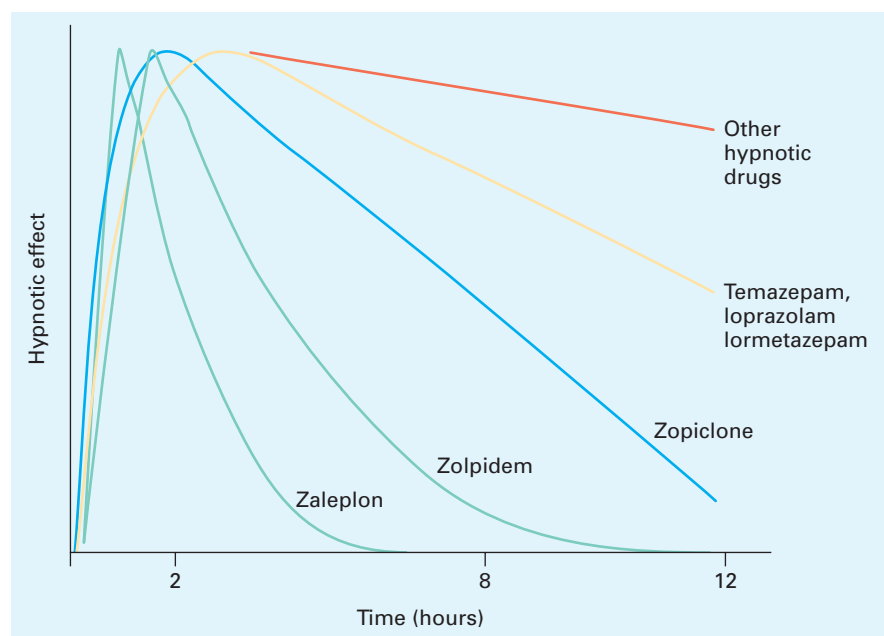


Fig 2. Approximate duration of action of hypnotic drugs.

studies indicate decreased effects after 4–8 weeks, implying the development of some tolerance. However, the necessity for dose escalation in insomnia is rare. Both animal and human research has shown that brain receptors change in character in response to chronic treatment with benzodiazepines, and therefore will take time to return to premedication levels after cessation of medication. Features of withdrawal and dependence vary. Commonly, there is a kind of psychological dependence based on the fact that the treatment works to reduce sleep disturbance, and therefore patients are unwilling to stop. If they do stop, there can be relapse and original symptoms return. Also commonly, there can be a rebound of symptoms, with a worsening of sleep disturbance for one or two nights, with longer sleep onset latency and increased waking during sleep.

Other drugs

Older drugs. Chloral hydrate, chlormethiazole and barbiturates also enhance GABA function, but at high doses have the additional capacity directly to open the membrane chloride channel. This may lead to potentially lethal respiratory depression and explains their low thera-

peutic ratio. These drugs have less evidence base for efficacy than the newer hypnotics and also have a propensity for abuse/misuse. Thus, they are very much second-line treatments.

Gammahydroxybutyrate. A GABA analogue, gammahydroxybutyrate (GHB), works on a novel non-GABA-A receptor system in the brain. It is a powerful sedative/anaesthetic agent that is strongly sleep-promoting, but very short-lived in its hypnotic action. GHB is a class C controlled drug in the UK, more popularly known as 'GBH' or 'liquid ecstasy', abused by body builders and sometimes used for date rape. It has been known for many years that GHB is an effective treatment of cataplexy in narcolepsy, possibly because it consolidates rapid eye movement sleep. GHB should be licensed in Europe for this indication in 2005.

Antidepressants. There is no objective evidence that very low doses of tricyclic antidepressants improve sleep in primary insomnia. In depression, mirtazapine is useful in patients with marked insomnia as a symptom.

Melatonin. Melatonin, the hormone produced by the pineal gland during darkness has been investigated for insomnia

but it appears to be ineffective, although it seems to help in alleviating jet lag.

Over-the-counter medications. Most proprietary (over-the-counter) sleep remedies contain antihistamines. Promethazine reduces sleep onset latency and awakenings during the night after a single dose, but no studies have lasted longer than one night. There are few controlled studies showing improvements in sleep after other antihistamines. Most antihistamine sedatives have a relatively long action and may cause daytime sedation. There are very few randomised clinical trials of herbal sleep aids⁶ and so far evidence for efficacy is inconsistent.

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