Insomnia management

CPD

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Background
Insomnia is a common condition affecting individuals of various ages that can be addressed using a range of validated treatments.

Objectives
The aim of this review is to outline current treatment approaches for insomnia disorder.

Discussion
Current guidelines suggest cognitive behavioural therapy is the first-line treatment for insomnia. This may be complemented with short-term pharmacological intervention.

INSOMNIA DISORDER is characterised by inadequate sleep despite adequate sleep opportunity, accompanied by daytime dysfunction. Both pharmacologic and psychological interventions are indicated for the treatment of insomnia disorder; however, selecting the right treatment is dependent on the chronicity of symptoms, with medical and psychiatric factors taken into account. The Australasian Sleep Association (ASA)[1], American Academy of Sleep Medicine[2], American College of Physicians[3] and European Sleep Research Society[4] all recommend cognitive behavioural therapy for insomnia (CBT-I) as the first-line treatment for patients with insomnia disorder.

Patients presenting with acute symptoms of insomnia may benefit from short-term medication in concert with sleep hygiene education.[5] However, patients prescribed medications for short-term use require close monitoring for medication dependence, psychiatric status, unproductive sleep-specific coping strategies and maladaptive cognitions, as well as the severity of stressors, as these factors may precipitate and perpetuate insomnia.

Cognitive behavioural therapy for insomnia

CBT-I refers to a range of evidence-based techniques packaged into a multiple-session treatment that includes behavioural and cognitive strategies (Box 2). Invariably, CBT-I includes all of these components, delivered over several sessions by a psychologist or trained healthcare professional.

Meta-analysis of randomised controlled trials (RCTs) shows unequivocally that CBT-I reduces sleep onset latency and nocturnal arousals while improving sleep efficiency (ie the length of time asleep relative to the amount of time spent in bed), with effect sizes comparable in magnitude to hypnotics such as benzodiazepines and non-benzodiazepines.[6] Unlike hypnotics, improvements in sleep following CBT-I are maintained after treatment cessation for up to three years.[7] Improvements in sleep have also been observed in patients prescribed CBT-I in combination with temazepam[8] and zolpidem[9]; however, sleep improvements are better maintained in patients who are not medicated.

Stand-alone CBT-I is safe and well tolerated by a large number of clinical populations. The possibility of manic

states precipitated by sleep restriction in patients with bipolar illness has been raised, and one study found CBT-I resulted in mild increases in hypomania.[10] Sleep restriction in patients with sleep apnoea should be used judiciously given that it can worsen daytime sleepiness and vigilance.[11] Consultation by a sleep specialist may be necessary to investigate and treat sleep comorbidities that may co-exist or mimic insomnia (refer to Box 1). Sleep restriction can be used to increase sleep pressure in lieu of the sedating properties of hypnotics, though this may worsen daytime sleepiness, particularly when combined with medications with a long half-life.

CBT-I is dependent on trained clinicians, which limits accessibility.[5] CBT-I can be time-consuming (typically 4–8 weeks), which may be difficult for time-poor individuals; however, online interventions such as Sleepio, SHUTi, and CBT-I Coach may circumvent the logistics associated with face-to-face delivery.[12] Meta-analyses suggest online programs are comparable to face-to-face delivery.[13] Other insomnia treatments such as sleep-specific relaxation, music or white noise applications have not been validated against CBT-I. Mindfulness combined with CBT-I has been found effective in treating insomnia[14] and is now an intervention endorsed by the ASA.[1] A recent meta-analysis suggests that exercise improves subjective sleep quality in insomnia disorder;[15] however, the literature is limited and larger studies are required before it is incorporated into behavioural interventions.

Pharmacological management of insomnia

The ASA now recommends that 'CBT-I should be used whenever possible, and medications should be limited to the lowest necessary dose and shortest necessary duration.'[1] However, the ASA acknowledges that pharmacological intervention is necessary in some circumstances.

Hypnotic medication may be useful for patients who have short-term bouts of insomnia (ie insomnia symptoms lasting <4 weeks) while simultaneously treating underlying causes (eg vocational, educational, parental or personal stressors, or illness).[16] Short-term insomnia may respond to sleep medication with sleep hygiene;[2] however, patients with persistent symptoms lasting >3 months will likely benefit from a multifaceted treatment approach that involves CBT-I as well as treatment of comorbid medical and psychiatric factors. The main limitation of sleep medication is its lack of long-term effectiveness, particularly for patients with insomnia disorder, given the paucity of long-term trials beyond 12 months.[16] Most sleep medications are not approved for use beyond three months, and hypnotics are only indicated for four weeks.[16]

Selecting the right medication is dependent on the type of insomnia symptoms (ie difficulties initiating sleep versus sleep maintenance).[16,17] Patients presenting with sleep onset difficulties may benefit from quick-onset medications with a short half-life (eg temazepam, zolpidem, zopiclone), whereas patients waking after a few hours of sleep may require longer-acting medications (eg nitrazepam, oxazepam).[12] Unfortunately, the drawback of long half-life sleep medications is the risk of residual sedation. Sleep-wake circadian rhythm – that is, whether it is advanced or delayed – is an important consideration, as patients presenting with circadian disruption secondary to shift work or genetic predisposition may benefit from appropriately timed melatonin.[16]

The potential benefits of pharmacologic intervention need to be balanced with

Box 1. Comorbidities and risk factors associated with insomnia

Sleep disorders
- Sleep apnoea
- Circadian rhythm sleep disorders
- Parasomnias
- Restless leg syndrome
- Periodic limb movement disorder
- Narcolepsy
- Nightmares

Psychiatric disorders
- Depressive disorders
- Bipolar and related disorder
- Anxiety disorders
- Post-traumatic stress disorder
- Personality disorders such as narcissistic and borderline

Prescription medications
- Antidepressants
- Adrenergic agonists (eg salbutamol, dexamphetamine, methylphenidate)
- Opioids
- Corticosteriods

Non-illicit substances
- Caffeine – determine frequency and ingestion relative to bedtime given caffeine's long half-life
- Coffee and black tea
- Energy drinks, gels, shots
- Electrolyte replacements
- Protein, meal/weight replacement shakes
- Alcohol – determine frequency and amount relative to bedtime

Medical

Respiratory
- Asthma
- Chronic obstructive airway disease

Cardiovascular
- Congestive heart failure
- Ischaemic heart disease

Endocrine
- Thyroid abnormalities
- Diabetes
- Menopause

Neurological
- Neurodegenerative conditions (eg Alzheimer's disease, Parkinson's disease)
- Neuromuscular disorders
- Traumatic brain injury
- Stroke
- Chronic pain
- Chronic fatigue syndrome

Lifestyle
- Shift work/long hours
- Excessive stimulant use

the side effects.[12] Hypnotics should be prescribed judiciously to those with alcohol dependency, pulmonary disease or sleep apnoea in light of the increased risk of excessive sedation and respiratory suppression.[12] Night shift workers may be vulnerable given the long half-life of some hypnotics, which can impair cognition.[12] Older individuals and patients with impaired renal and hepatic functioning are also vulnerable given that metabolic clearance may be delayed, resulting in excessive sedation.[12]

Specific sleep medications

In Australia, medications approved for the treatment of insomnia include benzodiazepines, benzodiazepine receptor agonists (referred to as 'Z-drugs') and dual orexin receptor antagonists. Other medications include sedative antidepressants, melatonin, antihistamines and calcium channel alpha-2 ligands.

Benzodiazepines

Benzodiazepines are the most commonly used and most widely prescribed sleep medication, and they include temazepam, nitrazepam, oxazepam and flunitrazepam. Meta-analysis of RCTs indicates benzodiazepines are effective in reducing sleep onset latency and increasing sleep duration.[18] Benzodiazepines have been found to result in daytime drowsiness and memory impairment.[18] They have also been found to exert an anxiolytic effect, which may be appropriate for patients with comorbid insomnia and chronic anxiety. The long-term dependency and tolerance of benzodiazepines are not well established, and it is important to exercise care when prescribing beyond the recommended short-term usage for insomnia withdrawal. Discontinuation of benzodiazepines is best achieved slowly. Morin et al found that reducing benzodiazepines by 25% every two weeks over a 10-week period was superior when complemented with CBT-I, compared with medication tampering alone.[19]

Non-benzodiazepines

Non-benzodiazepines preferentially bind to $GABA_A$ receptor subtypes and have a short half-life (between approximately two and six hours).[20] The most commonly used medications include zolpidem and zopiclone, which are collectively referred to as 'Z-drugs'. Non-benzodiazepines reduce sleep onset latency and waking after sleep onset while increasing total sleep time.[21]

Although Z-drugs are marketed as being safer than benzodiazepines because they carry a lower risk of dependence and morning sedation, there are no direct comparisons with comparable short-acting benzodiazepines to determine if these favourable effects are merely due to shorter duration of action or specificity of action. Common side effects of zolpidem include delirium, ataxia and memory

Box 2. Cognitive and behavioural components of cognitive behavioural therapy for insomnia

Behavioural strategies

Sleep restriction – The aim of sleep restriction is to increase sleep drive and reduce time awake in bed. Time in bed is limited to align with the patient's sleep duration. Gradually, more time is spent in bed as sleep improves. Sleep restriction is typically administered by trained professionals, and requires close monitoring of daily sleep–wake patterns.

Stimulus control – Behaviours that require wakefulness (eg watching TV, rumination) in bed could result in bed being associated with hyperarousal, thereby perpetuating sleep difficulties. Stimulus control helps to re-associate bed with being asleep, thereby reversing arousal.[32] Individuals are instructed to go to bed only when sleepy, and not when alert. This helps re-associate bed with sleepiness. Individuals limit activities in bed to only sleeping and sex, and carry out waking behaviours that may previously be associated with bed (eg using a mobile phone) outside of bed. Individuals are instructed to have a 'time out' if they are unable to sleep within what feels like 15–30 minutes (without looking at the clock). During the time out, individuals complete a non-stimulating task, returning to bed when they feel comfortable. The same rise-time is recommended even if sleep the night before is poor.

Both sleep restriction and stimulus control may cause increased daytime sleepiness in the short term. Monitoring and management of daytime sleepiness are important when administering either component.

Relaxation – Relaxation strategies can include progressive muscle relaxation and diaphragmatic breathing with the intent of addressing arousal.[33] The goal is to release tension and arousal; however, close monitoring of patients is important as relaxation may become sleep effort in disguise.[33]

Sleep hygiene – General behavioural and environmental strategies can help patients improve and maintain good sleep; however, sleep hygiene is insufficient for the treatment of insomnia as a standalone intervention.[33]

Facilitating circadian rhythm – Patients can be encouraged to adopt a regular sleep and wake schedule across weekdays and weekends to consolidate sleep and strengthen the circadian system. Optimising light exposure (natural or artificial) in the morning while limiting light exposure (eg electronic devices) in the evening helps with synchronising the human circadian system, given the known impact on melatonin production.

Cognitive strategies

Psychoeducation – It is important to educate the patient about sleep aims to address misconceptions about sleep. Some cognitive behavioural therapy for insomnia (CBT-I) programs encourage clinicians to use the Spielman model;[34] refer to the 'Theory and assessment of insomnia' insomnia model to educate patients about their other sleep behaviour and cognition, thereby forming a rationale for the other cognitive and behavioural strategies.[33]

Cognitive therapy – Cognitive therapy is geared toward teaching patients to be aware, identify, evaluate and respond constructively to their unhelpful thoughts and beliefs about sleep. It is incorporated throughout the program to complement behavioural strategies. Managing worries and anxieties before bed dampens psychological hyperarousal.[33]

Cost and availability

In Australia, CBT-I sessions are covered by a mental healthcare plan. Refer to the Australasian Sleep Association (ASA) service directory for treatment centers (www.sleep.org.au).

disturbance; however, these side effects have been observed with other sedatives, particularly in individuals who are stressed or drink alcohol. Therefore, it is unclear how the incidence of these adverse events compares with other sedatives.[22] It is recommended that discontinuation be gradual (eg reduction by 25% of the original dose every two weeks) and complemented with CBT-I.[17]

Dual orexin receptor antagonists

Dual orexin receptor antagonists, also referred to orexin receptor antagonists, are a new class of medication purposefully designed for the treatment of insomnia,[12,16] with suvorexant being the first available treatment in Australia[16] and the US[12]. Suvorexant facilitates sleep via the binding inhibition of wake-promoting neurotransmitters orexin A and orexin B.[23] A multicentre placebo-controlled clinical trial found suvorexant improved subjective total sleep time and sleep onset latency.[24] Daytime somnolence was found to be the most common side effect after abrupt cessation following one year of treatment.[24] Suvorexant may be useful to treat patients with insomnia who have difficulties 'switching off'.[16] Dual orexin receptor antagonists may produce less delirium in the elderly, and trials are underway to measure efficacy and safety of these medications in patients with cognitive decline and co-existent insomnia.

Other sleep medications

Sedating antidepressants

Antidepressants are not approved for the first-line treatment of insomnia.[16] However, they may be useful for insomnia patients with comorbid depression given their anticholinergic, antihistaminergic, serotonergic and adrenergic antagonistic activity.[12,17] Antidepressants that may be useful include amitriptyline, doxepin, nortriptyline, mirtazapine and agomelatine.[16] In the US, doxepin has been approved for primary insomnia by the Federal Drug Administration at doses of 3–6 mg,[17] with improvements in sleep maintenance and total sleep time, and no evidence of rebound insomnia after 35 days in a controlled study.[25] A Cochrane review found that doxepin and other tricyclic antidepressants improved subjective sleep quality, sleep efficiency and increased sleep duration, with little impact on sleep latency.[26] Mirtazapine may also be prescribed for 'off-label' use for insomnia patients comorbid with depression,[17,27] although side effects can include rebound insomnia on discontinuation.

Calcium channel alpha-2 delta ligands

Antiepileptics such as gabapentin and pregabalin are being used for the treatment of insomnia.[16] Studies investigating gabapentin have observed improvements in sleep quality and reductions in nocturnal arousals after approximately four weeks.[28]

Melatonin and agomelatine

In Australia, the only retail prescription melatonin preparation available is Circadin, an extended-release formula approved for insomnia patients aged >55 years, in whom clinical trials have found improvements in sleep quality and sleep efficiency.[29]

Agomelatine is a synthetic melatonin receptor agonist, with antagonism of the serotonin 5-HT2C receptor providing an additional antidepressant effect. It is equally as efficacious as other antidepressants but has greater tolerability in terms of sleep-related side effects,[30] so it is sometimes used for combined mood and sleep disturbance. As a result of cost and limited comparative data around efficacy, it is rarely used to replace melatonin for isolated sleep disturbance.

Antihistamines

Over-the-counter antihistamines such as promethazine and doxylamine[16] have often been used by individuals before seeking specialist treatment. There is little evidence that antihistamines relieve insomnia, and they are not recommended.[12] Given their long half-life (resulting in next day somnolence) together with quickly developing tolerance,[31] their effect on relieving insomnia can wear off quickly,[16] potentially exacerbating daytime functioning impairments over and above the effects of insomnia alone.

Conclusion

Insomnia is a multifaceted sleep disorder that affects a large proportion of individuals and results in self-perceived dissatisfaction with sleep and concomitant effects in daytime functioning. Current guidelines recommended that patients with transient symptoms of insomnia be managed conservatively with a combination of pharmacologic and behavioural interventions. The cost–benefit ratio of pharmacologic intervention must be weighed, taking into account the patient's psychiatric, medical and substance-use history. Overwhelming evidence from multiple clinical trials now indicates that insomnia disorder is best treated using CBT-I, though this may be complemented with pharmacologic intervention. CBT-I may also be used to help with sleep medication cessation. Given the complexity of insomnia disorder, multidisciplinary sleep clinics involving sleep physicians and psychologists are being established in Australia to treat insomnia and simultaneously treat comorbidities. Effective insomnia treatment requires a multidisciplinary team that is centred on the patient's preference and personal goals.

Key points

- Bouts of insomnia occurring for <3 months can be treated pharmacologically, though ongoing monitoring is necessary.
- Insomnia disorder occurring for >3 months is best treated and managed using CBT-I.
- CBT-I can be used to help patients wean off hypnotics.

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