abstract

Chronic insomnia is common among older adults and has significant negative consequences for health and well being. A comprehensive approach to treatment begins with identification and management of any underlying conditions. Treatment of insomnia includes both non-pharmacologic and pharmacologic options. Non-pharmacologic approaches form the foundation of treatment; hypnotic medications can also be effective but may be associated with adverse drug effects. Zopiclone and zaleplon appear to be associated with fewer side effects than benzodiazepines.

Key words: insomnia, older adults, drug therapy, behavioural therapy, hypnotics

Insomnia in Older Adults, Part II: Treatment

Amit Morris, BSc, School of Medicine, Queen's University, Kingston, ON; Department of Psychiatry, Sleep and Alertness Clinic, Toronto Western Hospital, University of Toronto, Toronto, ON.

Henry J. Moller, MD, FRCP(C), DABSM, Department of Psychiatry, Sleep and Alertness Clinic, Toronto Western Hospital, University of Toronto, Toronto, ON.

Colin M. Shapiro, MBBCh, PhD, FRCP(C), Department of Psychiatry, Sleep and Alertness Clinic, Toronto Western Hospital, University of Toronto, Toronto, ON.

Introduction

Insomnia—defined as difficulty falling asleep or staying asleep, or unrestorative sleep—is very common among older adults and is associated with significant negative effects on health, as well as decreased quality and length of life (see previous article in this series).[1] Recent evidence suggests that this may be a consequence of loss of neurons in the ventrolateral preoptic nucleus.[2] In animals, lesions in this area lead to more frequent but shorter bouts of sleep—resulting in a reduction in overall sleep time—as well as poorer sleep quality. This is similar to the sleep pattern of many older adults.

Because medical and psychiatric disorders as well as drug side effects are frequent causes of sleep problems in older adults, a thorough assessment is essential. The first step in treatment is to address any such underlying conditions. Numerous drugs can induce insomnia (see previous article in this series);[1] changing medication or the time of administration may alleviate the problem. Alternatively, insomnia may be a primary disorder, without another condition or substance as its apparent cause. While an occasional disrupted night is normal, ongoing sleep difficulties—especially if they occur more than a couple of nights per week—merit intervention. The aim of intervention is to achieve both a treatment benefit (with an impact on quality of life) and a preventative effect (e.g., decreasing the subsequent chance of a depressive episode).

The previous article in this series discussed the prevalence and etiology of insomnia among older adults and provided an approach to its evaluation in a primary care setting.[1] This article will review both pharmacologic and non-pharmacologic treatment options.

Pharmacologic vs. Non-Pharmacologic Treatment

Non-pharmacologic therapies form the foundation of treatment for chronic insomnia, especially in older adults. A non-pharmacologic approach is not associated with the risks of drug therapy, such as tolerance, dependence, "hangover" effects, substance-induced changes in sleep architecture, and medication interactions. Complications of drug therapy are both more likely and more problematic in older adults due to age-related changes in pharmacokinetics and pharmacodynamics, as well as comorbidities, polypharmacy, and increased susceptibility to falls and fractures. Non-drug therapies are often effective[3] and can produce lasting improvements in sleep.[4] Indeed, gains due to non-pharmacologic therapy may be better maintained than those achieved with the use of hypnotics.[4]

Newer non-benzodiazepine hypnotics (e.g., zopiclone, zaleplon) have better side effect profiles than benzodiazepines (BZs) and have improved the

options for pharmacologic management. However, they—like BZs—are typically still recommended for short-term use only.[5,6] Our view is that long-term therapy is warranted in some patients, given the negative effects of chronic sleep problems (see below).

Non-Pharmacologic Therapy

A number of non-pharmacologic insomnia treatments have been developed; these can be combined with each other and / or pharmacologic therapy.

Sleep Hygiene

Attention to sleep hygiene is an important part of any insomnia intervention. Sleep hygiene involves commonsense principles aimed at ensuring that both behaviours and environment are conducive to night-time sleep. Table 1 lists some instructions for patients. A regular bed- and wake-time is the cornerstone of good sleep hygiene. Note that while alcohol is commonly used as a sedative, it decreases sleep quality and increases sleep fragmentation.[7] Regular exercise and social activity are extremely important: one study of over 13,000 individuals found that inactivity and dissatisfaction with one's social life were strong predictors of insomnia. After controlling for these factors, older age alone did not predict insomnia.[8] Activity and a satisfying social life tend to be "sleep-protective" at any age. Exercise has been shown to improve both sleep and depressive symptoms in older patients.[9,10]

Stimulus Control or "The 20-Minute Rule"

Individuals with insomnia often come to associate bedtime rituals and features of the sleep environment with difficulty sleeping, thereby perpetuating the sleep problem. If unable to sleep after about 20 minutes—either upon initially retiring or after awakening during the night—the patient should get out of bed and do something relaxing and slightly boring until sleepy (i.e., no stimulating TV programs). This can be repeated as necessary. The aim is to associate the sleep environment with falling asleep quickly.[11]

Table 1: Sleep Hygiene Rules

Engage in quiet activities and avoid stimulating activity just before bedtime
Do not go to bed until you are sleepy
Reserve the bed for sleeping and sex; do not read or watch TV in bed
Get up at the same time each morning and go to bed at the same time each night, including weekends
Avoid naps if they disrupt sleep the following night; otherwise, limit them to the early afternoon
Get regular exercise and enjoy regular social activity (but avoid strenuous activity after 6 p.m.)
Eliminate or minimize alcohol use; do not drink alcohol within two hours of bedtime
Eliminate or minimize caffeine use; do not consume caffeine after 4 p.m.; especially sensitive individuals should avoid caffeine after noon
Eliminate or minimize smoking; do not smoke within four hours of bedtime
A light carbohydrate snack may promote sleep; avoid heavy meals before bedtime. Milk, bananas, and turkey contain tryptophan, which promotes sleep
The sleep environment should be comfortable, without being too warm, and should admit minimal light and noise

Source: Adapted from Fleming and Shapiro,[11] Chilcott and Shapiro,[13] and Sloan *et al.*[38]

Bed Restriction

This strategy is particularly pertinent in older adults, many of whom go to bed early and stay in bed too long. It requires that the patient keep an ongoing sleep diary. Because excessive time in bed can perpetuate insomnia, time in bed is restricted to equal the total sleep time previously recorded by the patient. Rising time is based on his / her usual schedule, and bedtime is set accordingly, but not so as to allow less than 4.5 hours of sleep. Once sleep efficiency (sleep time = time in bed) reaches 0.90 for one week, the patient may retire 15 minutes earlier. Bedtime is adjusted up or down by 15 min / week to maintain sleep efficiency between 0.85 and 0.90.[11] Notably, sleep efficiency appears to be important for subjective satisfaction with sleep.[12]

Progressive Relaxation

To promote a sense of relaxation, patients may alternately tense and relax each of the major muscle groups, or imagine their body parts being immersed in warm water or covered with warm blankets.[13]

Cognitive Approaches

Identifying and replacing maladaptive thoughts can aid in defusing anxiety associated with sleep disturbance. For example, "catastrophic" expectations about the effects of a poor night's sleep on daytime function can be replaced by less distressing, more realistic expectations,[11] namely, that they may feel fatigued but will not "go crazy," be totally incapacitated, etc.

Group Therapy

Kupych-Woloshyn *et al.* have described an effective group therapy approach to the treatment of severe chronic insomnia.[14] Potential benefits of this method include a decreased sense of isolation, increased support and the opportunity for collective problem-solving, didactic learning, and sharing of effective techniques. Treating several individuals at once makes this a cost-effective strategy; therapists skilled in leading groups using evidence-based treatments are becoming more common in current fiscally strained Canadian medical environments.

Table 2: Recommended Doses and Half-Lives of Several Hypnotics

Drug	Recommended Dose in Older Adults (mg)	Half-Life (hrs)
Benzodiazepine receptor agonists		
Zopiclone	5–10	5
Zaleplon	5–10	1
Benzodiazepines		
Lorazepam	0.5–2	10–20
Oxazepam	15–30	5–15
Temazepam	15–30	10–20
Clonazepam (for restless leg syndrome or periodic leg movements in sleep)	0.5–2	20–80

Source: Adapted from Canadian Pharmacists Association[27] and Fankhauser.[39]

Light Therapy

A "phase-advanced" sleep-wake cycle is common among older adults and may result in early morning awakening and early evening sleepiness. Bright light in the evening can help correct the disparity between the patient's circadian rhythms and his/her desired sleep-wake times. Light therapy may also mitigate the profoundly disrupted sleep-wake rhythms and nocturnal agitation ("sundowning") common in Alzheimer's disease. Older adults should try to spend time outside as late during daylight hours as possible.[15] Phototherapy supplementation with a light box may be necessary. A "light book" is a small device that emits light at a wavelength that specifically suppresses melatonin release; it may be particularly effective and convenient for older adults. Mild exercise and regular social activity may help further entrain sleep-wake rhythms and so benefit individuals experiencing sundowning or advanced sleep phase.[16]

Education

It is also important that the patient understands that sleep quality does decrease naturally with age. This is certainly not to suggest that a sleep concern be overlooked, only that expectations must be realistic. To use an analogy: an older person who does not expect to be able to lift the same amount of weight he/she could at 20 years of age may still expect to have the sleep of a 20-year-old.

Pharmacologic Therapy

Although non-pharmacologic treatments are effective and associated with few side effects, pragmatic considerations often lead to the use of hypnotic medications in older adults. Hypnotic medications can be effective for the short-term treatment of insomnia.[6] Although none of the hypnotic agents currently available is typically recommended beyond short-term use, perhaps 20% of patients with severe insomnia require long-term hypnotic therapy in order to improve quality of life and avoid adverse consequences of sleep disturbance. This is often inappropriately handled by treating with antidepressants, which can be less safe and less effective, but may not carry the stigma of prescribing true hypnotics.

Moreover, standard advice is that hypnotics should be taken intermittently to decrease the chance of developing dependence.[6] However, from considerable experience, one of us (CS) believes that intermittent dosing can set up a conditioning paradigm, leading to more long-term use. Therefore, an eight-week course of one of the newer hypnotics is recommended for fragmented sleep. Eight weeks is chosen because there is some (albeit slight) evidence that this is the duration required for sleep restoration to occur. A critical component of therapy with hypnotics is a cautious tapering of the medication once satisfactory sleep is restored.

The major hypnotics for use in older adults include BZs and non-BZ benzodiazepine receptor agonists (e.g., zopiclone, zaleplon). Recommended doses for older adults and half-lives are presented in Table 2. Some suggested treatment strategies based on the patient's specific sleep disturbance are presented in Table 3.

Risks and Benefits of Pharmacologic Therapy

As mentioned above, pharmacologic therapy for insomnia carries associated risks. Appropriate selection and dosing of medications can help decrease these risks. Side effects of the newer agents zopiclone and zaleplon, while not absent, appear to be less frequent and less pronounced than with BZs.[6] As always, it is necessary to weigh the risks and benefits of therapy against those of the untreated condition; like hypnotic medications, insomnia itself is associated with daytime cognitive impairment and risk of accidents or injury.[17] Sleep disturbance has been shown to be a strong predictor of future depression in non-depressed community-dwelling older people,[18] and insomnia increases the suicide risk of individuals with severe psychiatric illness.[19]

Benzodiazepines

Although BZs have been used as hypnotics since the 1960s, they exhibit several potential side effects which limit their utility, including tolerance, dependence, "hangover" effects in the daytime, mild depression of respiratory function, and disruption of sleep architecture—especially suppression of slow wave and rapid eye movement (REM) sleep (reviewed by Montplaisir *et al.*).[6] They occasionally cause paradoxical agitation and have additive effects with alcohol and other CNS depressants. The side effect profiles of these agents vary with the duration of action of the primary drug as well as any active metabolites. Very short acting benzodiazepines can

cause daytime anxiety and "rebound" or "recoil"[20] insomnia upon discontinuation, while long-duration BZs can cause residual daytime sedation and are not suitable for use in older adults.[11] The most appropriate choice of BZ for older adults is therefore often one with a short / intermediate duration of action. As BZs have anxiolytic as well as hypnotic properties, short-term BZ therapy may be indicated for treatment of transient insomnia associated with anxiety. Restless leg syndrome, periodic leg movements in sleep, and parasomnias are other sleep problems in which a BZ may be preferable to newer agents.

Zopiclone and Zaleplon

Zopiclone and zaleplon (as well as zolpidem, which is not currently available in Canada) are more recently developed short-duration hypnotics. The more favourable side-effect profiles of these drugs compared to BZs make them the preferred hypnotics for older adults.[21] These agents are associated with less tolerance, dependence and rebound / recoil insomnia, "hangover" effects, respiratory impairment, and disruption of sleep architecture than are BZs.[6]

Zopiclone has been shown to have hypnotic properties equal or superior to BZs (as reviewed in Montplaisir *et al.*).[6] It is useful for patients who have difficulty falling or staying asleep. Because it does not seem to alter respiration in pulmonary disease, zopiclone is recommended over BZs for all patients with impaired breathing, including chronic obstructive pulmonary disease, sleep apnea, increased upper airway resistance, and snoring.[6] For patients using BZs chronically, the substitution of a short course of zopiclone for the BZ has been shown to facilitate BZ cessation and prevent rebound insomnia.[22,23] Eventual discontinuation of zopiclone is then possible with less rebound insomnia. There is some evidence of residual sedation and impaired driving the morning after using zopiclone.[24,25] As with BZ, it is prudent to be aware of potential interaction with alcohol.

Given its short half-life (see Table 2), zaleplon is effective at initiating sleep but less effective at increasing sleep duration or preventing awakenings.[6] It is therefore suitable for the treatment of sleep-onset insomnia. Zaleplon appears to cause less residual sedation than either zopiclone or the short-acting BZs.[24,26] It is also possible to utilize zaleplon for middle-of-the-night awakenings—up to four hours before rising time—without causing residual daytime sedation.[26,27]

Zopiclone and zaleplon suppress slow-wave sleep less than do BZs.[28] Slow-wave sleep is key to the restorative aspect of sleep and is already in short supply in older adults.

Melatonin

Melatonin is a nocturnally secreted hormone involved in regulating circadian rhythms. Its secretion is disrupted with aging, especially among individuals with Alzheimer's disease.[29,30] While data are conflicting, a recent systematic review suggests that melatonin supplementation may be beneficial in some older adults.[31] If considering such treatment, a cautious approach would be to refer the patient for a dim light melatonin onset profile (DLMO) to ascertain if there is an abnormality of hormone release.

Tryptophan

If behavioural therapies appear to be insufficient, but a patient is ambivalent about taking medications, tryptophan may be an option. Some people prefer to take this sleep-promoting substance—which is found in foods such as milk, cheese, tuna, and turkey—over hypnotics, which are perceived as less natural. Data are conflicting; however, there is evidence that certain individuals' sleep disturbance responds to tryptophan supplementation.[32,33]

Other Drug Classes

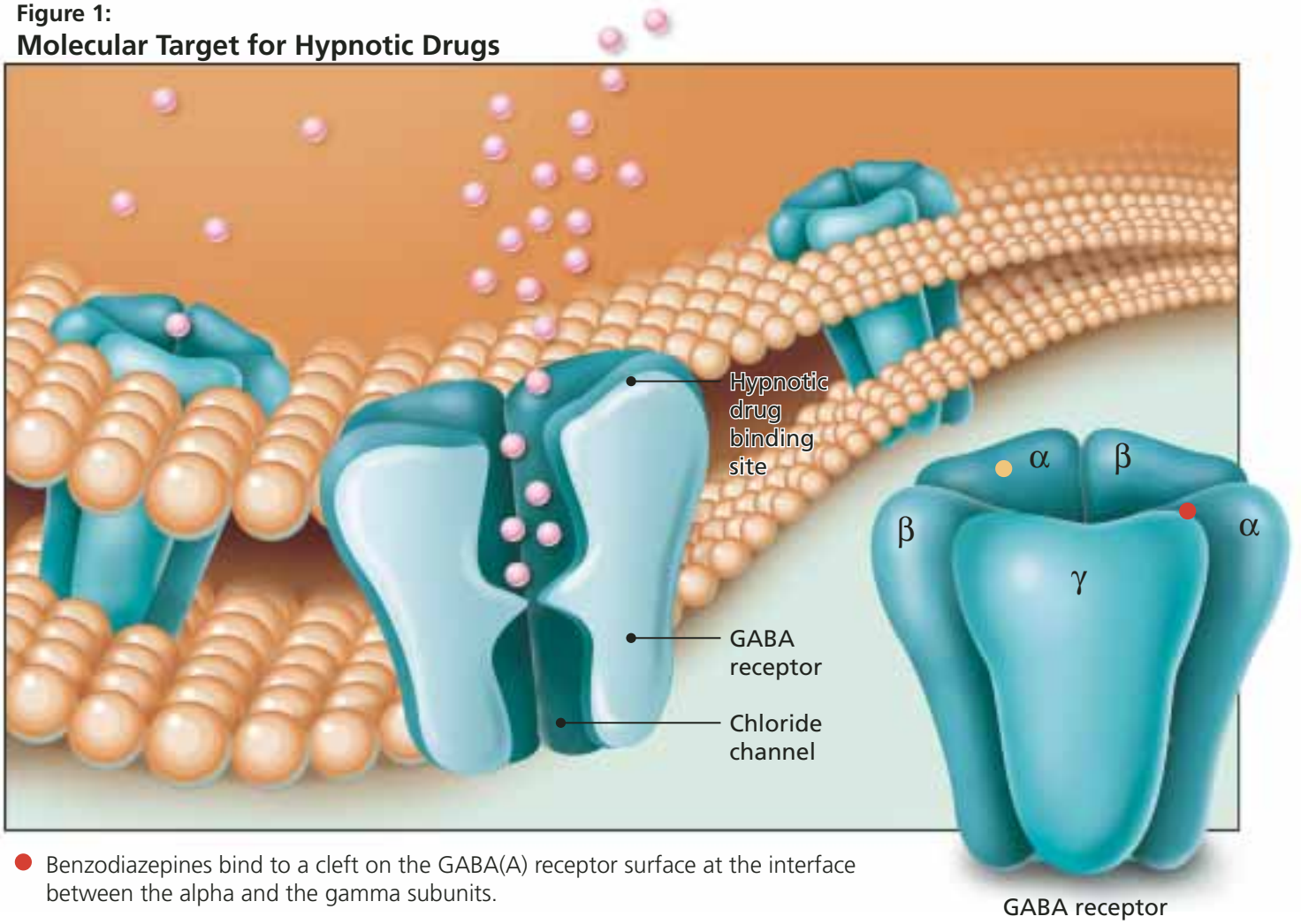
Generally, pharmacologic treatment of insomnia should employ a hypnotic rather than utilizing the side effects of another drug class.

Although the use of sedating antidepressants (e.g., trazodone, amitryptiline) to treat insomnia is prevalent, they are not particularly effective in non-depressed

Table 3: Recommended Treatment Strategies by Sleep Problem

Sleep Problem	Recommended Strategies
Individual spends too much time in bed	Consider bed restriction
Fragmented sleep (i.e., multiple arousals) or problems falling asleep at the start of the night	Eight-week course of zopiclone (with review two weeks after cessation) or exercise or cognitive therapy
Insomnia related to restless leg syndrome and/or periodic leg movements in sleep (bed partner complains of kicking)	Incremental dose of clonazepam 0.5–2mg or caffeine/nicotine withdrawal (other non-hypnotic medications, e.g., selegiline, pramipexole, or L-dopa, may be useful)
Middle-of-the-night awakening with difficulty falling back asleep	Zaleplon as needed—can be taken up to four hours before rising time
Difficulty falling asleep associated with anxiety (transient/situational)	Temazepam/lorazepam/clonazepam as needed (short-term/ occasional use)
Insomnia associated with depression	Sedating antidepressant (e.g., mirtazapine) or cognitive therapy, if appropriate

Figure 1:
Molecular Target for Hypnotic Drugs



- Benzodiazepines bind to a cleft on the GABA(A) receptor surface at the interface between the alpha and the gamma subunits.
- Other drugs (zopliclone, zolpidem) also bind to the alpha subunit, but interact with amino acids in distinct binding domains to the benzodiazepines.

patients and are associated with potentially dangerous anticholinergic, hypotensive, and other side effects.[34] However, if the insomnia is indeed associated with depression, sedating antidepressants may address both issues; mirtazapine has recently been shown to be effective at treating sleep disturbance associated with depression.[35]

Antihistamines in over-the-counter sleep agents and antiemetics can cause confusion, residual sedation, anticholinergic side effects (including urinary retention), and—rarely—hallucinations, and are not recommended.

For treatment-refractory insomnia, low doses of atypical antipsychotics may be effective sleep-promoting agents but are under-researched for this indication.[17] There is some anecdotal evidence that this class of drugs is helpful in Alzheimer's disease.[36]

There is also growing interest in the use of tiagabine, an antiepileptic agent, which acts as a selective GABA reuptake inhibitor (SGRI). Its purported advantages in older adults include increasing sleep efficiency, decreasing wakefulness during the night, and increasing slow-wave sleep.[37] This drug may be better at decreasing awakenings and increasing sleep quality than at helping people fall asleep.

Summary

Treatment of insomnia in older adults begins with a thorough assessment. Underlying causes should be sought and addressed; the patient's current medications should be reviewed for sleep-disrupting agents (e.g., SSRIs). Non-pharmacologic treatments for insomnia are numerous and can provide lasting benefit without side effects. Bed restriction is often especially helpful in older adults. Hypnotic medications can be beneficial, but classical teaching is that these drugs should not be used beyond short-term therapy. Our view is that ongoing treatment may be necessary, requires regular review, and will be enhanced by a formal sleep assessment. Zopiclone and zaleplon may be preferred over short or intermediate duration BZs due to their more favourable side effect

profiles. In selected cases with psychiatric comorbidity, other drugs may be helpful. Newer drugs should help physicians move away from prescribing older sedating antidepressants for sleep. u

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