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STATE OF THE ART REVIEW

Advances in the management of chronic insomnia

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ABSTRACT

Chronic insomnia is a common condition that affects people worldwide and has negative effects on patients' health and wellbeing. The treatment of insomnia can be complex and time consuming for patients and providers. Although behavioral interventions are the first line therapy, there are barriers to access for these treatments. However, in recent years, alternative ways of providing these behavioral therapies that make them more widely available have been investigated. Drugs also play an important role in the treatment of insomnia and new drugs have been introduced as options for treating patients with sleep initiation and sleep maintenance insomnia. In this review, we will discuss advances in the past six years in both non-pharmacologic and pharmacologic treatments for patients with chronic insomnia. We will also review the controversies surrounding some of the current drug treatments, as well as the role that technology and personal activity monitoring devices may play in treating insomnia.

Introduction

Over the past six years the management of chronic insomnia and short term insomnia has changed considerably. The *International Classification of Sleep Disorders, Version 3* (ICSD-3) defines chronic insomnia as having one of the following problems for at least three days a week for at least three months:

- Difficulty initiating sleep
- Difficulty maintaining sleep
- Waking earlier than desired
- Resistance to going to bed on appropriate schedule
- Difficulty sleeping without a parent or caregiver.[1]

Patients with short term insomnia have similar problems but for less than three months' duration (see fig 1 for summary of features of insomnia). Treating insomnia can be challenging because both pharmacologic and non-pharmacologic options have their limitations.

The efficacy of cognitive behavioral therapy for insomnia (CBT-I) remains undisputed, but problems with accessibility and cost effectiveness mean that many people with chronic insomnia do not benefit from this treatment. Therefore, alternatives and new ways of disseminating it to a wider patient population have recently been developed. Newer pharmacological treatments that target receptor systems other than $GABA_A$ (γ-aminobutyric acid) have also become available. Some of these seem to have different efficacy and potentially better safety and dependence profiles. The overall safety of long term use of sedative hypnotics, particularly $GABA_A$ agonists and antihistamines, has also come under scrutiny because of several longitudinal studies associating it with various chronic comorbidities and increased mortality, and this will also be outlined here. Lastly, the popularity of personal activity monitors with their various algorithms has changed the way chronic insomnia is managed by enabling patients to monitor their own progress.

This review will discuss the efficacy and shortcomings of various ways to deliver CBT-I and newer, non-pharmacological alternatives. It will also consider newer

LIST OF ACRONYMS

CBT-I: Cognitive behavioral therapy for insomnia
cCBT-I: Computerized and online cognitive behavioral therapy for insomnia
$GABA_A$: γ-aminobutyric acid
gCBT-I: Group cognitive behavioral therapy for insomnia
HRSD: Hamilton rating scale for depression
ICSD-3: *International Classification of Sleep Disorders, Version 3*
IRT: Imagery relief therapy
ISI: Insomnia severity index
LPS: Latency to persistent sleep
MBSR: Mindfulness based stress reduction
MBTI: Mindfulness based therapy for insomnia
PSAS: Pre-sleep arousal scale
PSQI: Pittsburgh sleep quality index
RCT: Randomized controlled trial
SOL: Sleep onset latency
TAU: Treatment as usual
tCBT-I: Cognitive behavioral therapy for insomnia through telehealth
TSO: Time to sleep onset
TST: Total sleep time
WASO: Wake after sleep onset

Types of insomnia (ICSD-3)	Essential features	Duration of symptoms	Predisposing and precipitating factors
Not clearly defined but probably similar to short term and chronic insomnia	• Despite adequate time for sleep, frequent and persistent difficulty initiating or maintaining sleep • Distress about poor sleep or impairment in quality of life (or both)	• Symptoms for 3+ days/week • At least 3 months of symptoms	• Stress (eg work, relationships, death) • Personality features: anxiety, preoccupation with health concerns • Comorbid psychiatric conditions (eg mood disorders, anxiety disorders) • Comorbid sleep disorders (eg RLS) • Comorbid medical problems (eg GERD, chronic pain conditions, alcohol misuse) • External factors (eg cramped living quarters, undesirable sleeping environment) • Poor sleep hygiene (eg watching TV in bed)
Short term insomnia (acute insomnia, adjustment insomnia)	• Despite adequate time for sleep, short term difficulty with initiating or maintaining sleep • Distress about poor sleep or impairment in quality of life (or both)	• Symptoms present for <3 months • May occur episodically and coincide with stress or a known precipitant	• Acute, identifiable stressor (eg relationship stress, occupational stress, bereavement, personal loss, new sleep environment) • Overall, similar to chronic insomnia factors
Other insomnia disorder	• Reserved for patients who have difficulty initiating or maintaining sleep but do not meet the full criteria for chronic insomnia disorder or short term insomnia disorder	• Diagnosis is non-specific and is used sparingly	• Not clearly defined but probably similar to short term and chronic insomnia

Fig 1| Features of insomnia GERD=gastroesophageal reflux disease; RLS=restless legs syndrome

pharmacological agents and those in the pipeline, the controversies surrounding sedative hypnotic drugs (sleep aids), and the conflicting evidence about the long term use of sedative hypnotics.

Incidence and prevalence

The prevalence of both acute and chronic insomnia in multinational cohort surveys has varied from 3.9% to 22%, depending on the definition used and the age group studied.[2-6] When using the ICSD-3 diagnostic criteria the prevalence of chronic insomnia is 9%[7 8] to 12%,[3 9] with transient symptoms of insomnia reported in 22-35% of the population.[3-10] The incidence of chronic insomnia in community dwelling adults in the United States, United Kingdom, and Taiwan has been reported to be 2.3-7.3% per year.[11-13] It is also a costly disease, in both healthcare utilization and absenteeism,[14 15] and it is associated with an increased risk of mortality (adjusted hazard ratio 1.58-2.74)[16 17] and statistically significant risk of morbidity. Disorders that are associated with an increased risk of insomnia include heart disease,[18-21] depression,[19-24] stroke,[25] hypertension,[26-28] dyslipidemia,[28 29] obesity,[19] and anxiety.[19 23] Chronic insomnia is also associated with an increased risk of car crashes, as well as injuries at home and at work.[30]

Sources and selection criteria

We identified studies for this review primarily through a search of English language publications listed on PubMed from 1 January 2010 until 31 January 2016. We chose these dates because most of the recent innovations in the treatment of insomnia and the controversies associated with it occurred during this time period. We used PubMed's controlled vocabulary terms (MeSH) and Medline's multi-field search for insomnia AND treatment, insomnia AND management, and insomnia AND therapy as well as the individual keywords sedatives, hypnotics, CBT-I, mindfulness, meditative movement, zolpidem, benzodiazepines, eszopiclone, doxepin, orexin, suvorexant, sleep tracking devices, insomnia treatment, and personal activity monitors. We limited the search to English language papers and included only prospective and retrospective case series, randomized controlled trials (RCTs), cohort studies, meta-analyses, and systematic reviews, choosing not to include case reports, opinion papers, and basic review articles. We also scrutinized additional studies included in the references of the original article list compiled.

Quality of evidence and limitations of literature

The scientific rigor of recent literature on the treatment of insomnia is quite robust. The evidence for the various non-pharmacologic treatments includes some well executed head to head trials for relative efficacy of each modality. The evidence on home monitoring devices suffers from lack of information on the various proprietary algorithms, but has reasonable comparative validity among devices, especially those that have been compared with objective clinical measures of sleep (such as actigraphy and polysomnography). The efficacy and safety of all pharmacological measures have been assessed by randomized placebo controlled trials, although most large trials were sponsored by the drug company that marketed the drug. In addition, no head to head trials have compared the efficacy of these drugs. Finally, it hard to draw conclusions from the retrospective case cohort studies on the safety of long term use of sedative hypnotics.

Non-pharmacologic management of insomnia

CBT-I is the mainstay of non-pharmacologic management of chronic insomnia. It has been repeatedly shown in RCTs to be superior to drugs in the treatment of chronic insomnia, both in efficacy and the duration of its therapeutic effects, using both subjective and objective polysomnographic criteria.[31-36] Table 1 provides details of these studies. CBT-I consists of sleep hygiene, stimulus control, sleep restriction, relaxation training, and cognitive restructuring,[37] and it has been shown to increase stages N2 and N3 and REM sleep and decrease wakefulness and stage N1, thus improving the regulation of sleep

Table 1 | Studies comparing CBT-I with drugs in the treatment of insomnia*

Drug	Population	Objective measure	Impact of cognitive behavioral therapy for insomnia
Sivertsen et al 2006[31]			
Zopiclone	46 older people† with insomnia	Polysomnography	Effect size (measured in Cohen's d) WASO 1.5 and 1.7 at 6 weeks and 6 months, respectively, with CBT-I *v* 0.1 and 0.2 with zopiclone SE 1.0 and 1.2 at 6 weeks and 6 months, respectively, with CBT-I *v* −0.1 and 0.0 with zopiclone Increase in N3 sleep 0.6 and 0.7 at 6 weeks and 6 months, respectively, with CBT-I *v* −0.4 and −0.5 with zopiclone
Wu et al 2006[32]			
Temazepam	71 adults with insomnia	Polysomnography	Compared with before treatment Mean decrease in SOL at 8 weeks, 3 months, and 8 months follow-up was 35.9 min, 38.9 min, and 32.8 min, respectively, with CBT-I *v* 44.9 min, 23.6 min, and 21.3 min with temazepam Mean SE at 8 weeks, 3 months, and 8 months increased by 9.2%, 14.6%, and 10.2% with CBT-I, respectively, *v* 14.3%, −2.9% and −1.9% with temazepam Mean TST at 8 weeks, 3 months, and 8 months increased by 21.6 min, 60.1 min, and 33.3 min, respectively, with CBT-I *v* 66.5 min, 32.4 min, −13 min with temazepam
Jacobs et al 2004[33]			
Zolpidem	63 young adults† with insomnia	Abbreviated home sleep monitoring	Before treatment measures compared with after treatment (6 weeks of CBT-I or zolpidem 10 mg for 4 weeks, 5 mg for 1 week, and 1 mg every other night for one week) Mean SOL improved by 15.5 min with CBT-I *v* 6.1 minutes with zolpidem Mean SE improved by 5.5% with CBT-I *v* 2.1% with zolpidemMean TST surprisingly decreased in both groups—by 2.6 min with CBT-I and 51.6 min with zolpidem
Omvik et al 2008[34]			
Zopiclone	46 older people† with insomnia	Daytime neuropsychologic testing	Effect size (Cohen's d) before and after treatment Reaction time: 0.46 with CBT-I *v* 0.21 with zopiclone Worry domain questionnaire: 0.4 with CBT-I *v* 0.14 with zopiclone State train anxiety inventory: 0.53 with CBT-I *v* −0.22 with zopiclone
Morin et al 1999[35]			
Temazepam	78 older people† with insomnia	Polysomnography	Mean values after 8 weeks of treatment WASO, SE, and TST improved by 32.41 min, 8.5%, and 6.8 min in CBT-I group, respectively, *v* 23.29 min, 6.56%, and 35.3 min in the temazepam group Follow-up with subjective measures (sleep diary) At 3, 12, and 24 months, improvement was maintained with CBT-I, whereas measures returned to pretreatment values at 12 months and 24 months with temazepam
McClusky et al 1991[36]			
Triazolam	30 adults with insomnia	No objective measures used; only outcome measures were subjective sleep questionnaires	Mixed model analysis of variance The 2 groups were compared at weeks 1, 2, 3, and 4 of treatment and 5 weeks after treatment. SOL: A significant week by treatment interaction and main effect for weeks emerged ($F=20.30$; df=4-112; $P<0.0001$ and $F=39.56$; df=4-112; $P<0.0001$, respectively). No significant difference at weeks 1 and 4. Triazolam group had significantly shorter SOL at week 2, while at 5 weeks after treatment the behavioral group had shorter SOL ($F=8.45$; df=1-28; $P<0.01$) TST: Both groups improved linearly over 9 weeks. CBT group increased from 6.33 h (standard deviation 0.71) to 7.15 h (0.74) ($F=31.88$; df=1-14; $P<0.0001$) and triazolam group increased from 6.57 h (0.62) to 6.84 h (0.80) ($F=5.48$; df=1-14; $P<0.01$)

*Abbreviations: CBT-I= cognitive behavioral therapy for insomnia; df=degrees of freedom; SE=sleep efficiency; SOL=sleep onset latency; TST=total sleep time; WASO=wake after sleep onset.
†Young adults: 19-64 years; older people: ≥65 years.

homeostasis.[38] RCTs comparing CBT-I with health education or no therapy have shown that CBT-I significantly improves insomnia that is comorbid with other conditions. These conditions include chronic pain,[39] arthritides,[40 41] migraine,[42] depression,[43-45] post-traumatic stress disorder,[46] cancer,[47-49] chronic obstructive pulmonary disease.[50] A case series found similar results in people with multiple sclerosis.[51]

However, CBT-I is not widely available because of the lack of local clinicians with specific training. Moreover, in the US for instance, CBT-I can be too expensive for patients and financially unsustainable for clinicians because of the complicated reimbursement system.[52] Therefore, there is much interest in alternatives to face-to-face CBT-I delivery as well as to CBT-I itself in the form of other non-pharmacologic treatments

Computerized and online CBT-I (cCBT-I)

A cost effective and accessible way to provide CBT-I is through online platforms that the patient can log into and go through the basics of CBT-I step by step. These are usually designed as six to eight week programs. When compared with other non-CBT treatments or no treatment, online CBT-I is superior in improving sleep efficiency or the percentage of time asleep out of time spent in bed, fatigue, mood, and overall daytime functioning.[53-56] The largest of these RCTs looked at 164 adults with chronic insomnia who were randomized to one of three arms: cCBT-I, imagery relief therapy (IRT: placebo), or treatment as usual (TAU). A sustained improvement in sleep efficiency was seen after six weeks of treatment with cCBT-I (20%) compared with TAU (6%; Cohen's d=0.95) and IRT (6%; Cohen's d=1.06), and this improvement was maintained eight weeks after treatment ended (20% *v* 7% for IRT (Cohen's d=1.00) and 9% for TAU (Cohen's d=0.69)). These findings were mirrored across a range of sleep diary measures. Sleep efficiency was >80% after six weeks of treatment in 76% of those in the cCBT-I group, 29% of those in the IRT group, and 18% of those in the TAU group. For >85% and >90% sleep efficiency, the corresponding figures were 55% and 38% of the cCBT-I group, 17% and 6% of the IRT group, and 8% and 0% of the TAU group; these improvements were largely maintained during follow-up.[53] When compared with face-to-face CBT-I, however, cCBT-I was inferior in both immediate improvement of insomnia and the longevity of the therapeutic benefits. Face-to-face CBT-I had a significantly greater treatment effect (Cohen's d=0.9)

on insomnia severity than cCBT-I at all time points. In addition, a moderate differential effect size favoring face-to-face treatment emerged at the three and six months' follow-up for all sleep diary estimates.[57] Overall cCBT-I also improved comorbid depression and anxiety (effect sizes −0.35, 95% confidence interval −0.46 to −0.25 for anxiety and −0.36, −0.47 to −0.26 for depression).[58] A meta-analysis of six RCTs found that cCBT-I does not consistently improve total sleep time (TST) (0.22, −0.03 to 0.46; I^2=0%) or wake after sleep onset (WASO) (−0.18, −0.43 to 0.06; I^2=55%).[59] However, it does have a high adherence rate (78%)[53 59] and a low number needed to treat (3.59).[59] A small randomized trial found that cCBT-I also significantly improved overall insomnia severity (P<0.001), sleep efficiency (P=0.002), sleep onset latency (SOL) (P=0.03), soundness of sleep (P=0.005), restored feeling upon awakening (P=0.002), and general fatigue (P=0.001) in cancer survivors with insomnia.[60] While cCBT-I is unlikely to be a replacement for in-person CBT-I, it is effective in mild to moderate cases of insomnia and its low cost and easy availability make it a viable alternative in certain patients. Its effect sizes (Hedges's g) on several variables at 0-6 weeks after treatment were 1.09 (insomnia severity), 0.58 (sleep efficiency), 0.45 (WASO), 0.41 (SOL), and 0.29 (TST), all of which were statistically significant.[61]

Group CBT-I

Group CBT-I (gCBT-I) allows a trained behavioral therapist to interact with and treat several patients with chronic insomnia. Each group is generally made up of five to eight participants, and the treatment involves five sessions delivered weekly or biweekly. Compared with unimodal behavioral interventions such as relaxation therapy[62] or treatment as usual,[63] gCBT-I improves the symptoms of insomnia (F=7.87; P=0.007) and the associated depressive symptoms (F=6.15; P=0.017),[62] with improvement being sustained for four to 40 weeks after treatment.[62] It has shown efficacy in various age groups, from adolescents[64] to older people.[65] gCBT-I is slightly more efficacious than cCBT-I in putting insomnia symptoms in remission at the completion of treatment (63% *v* 75%; P=0.24).[66] Adherence to gCBT-I is compromised by premorbid depression, poor therapeutic alliance, shorter sleep at baseline, and evening chronotype (propensity to go to sleep at or after 1 am and wake up at or after 9 am).[67-69] An RCT found that individual CBT-I was significantly better than gCBT-I in terms of SOL (P=0.001), sleep efficiency (P=0.001), and WASO (P=0.001).[70]

CBT-I through telehealth (tCBT-I)

Telehealth (video conferencing) is another low cost and easily accessible modality of delivering CBT-I. It has been shown to significantly improve sleep variables measured by sleep diaries and insomnia severity index (ISI) scores as well as symptoms of depression, as measured by the Hamilton rating scale for depression (HRSD), with statistically significant gains for two months after treatment. Effect sizes (negative values indicate a reduction from baseline and therefore improvement) were −1.10 for SOL, −2.03 for WASO, −1.64 for ISI, and −1.02 for HRSD.[71] There was no significant difference in insomnia symptoms or patients' preferences compared with people receiving cCBT-I, but the dropout rate was lower with tCBT-I (P<0.05).[72] There are no head-to-head comparison studies between face-to-face CBT-I and tCBT-I.

Dissemination of CBT-I to non-sleep specialists

The training of non-sleep specialists to provide CBT-I has had mixed results. Supervised training of nursing staff to deliver CBT-I in a general medical practice modestly improved insomnia measures in one RCT. Nurse delivered CBT improved SOL compared with TAU (P=0.002) but there was no significant difference between two groups at the six month follow-up. The same was true for WASO (P=0.001) and sleep efficiency (P<0.001) immediately after treatment, with no significant differences six months later.[73] Similarly CBT-I delivered by occupational health nurses showed a modest improvement in patients with mild insomnia (as measured by ISI) in two non-randomized group intervention trials.[74 75] A randomized controlled trial of manual guided CBT-I delivered in the primary care setting compared with no treatment showed modest but significant short term improvements in ISI scores (P=0.000), SOL (P=0.027), and WASO (P=0.027). However, therapeutic gains were not sustained 18 months after treatment.[76]

A pioneering training program within the US Department of Veteran Affairs (VA) health system in 2012 targeted mental health clinicians from different disciplines, including psychiatry, psychology, social work, and nursing, with the goal of expanding the number of clinicians who can practice CBT-I.[77] These clinicians were trained in the basics of CBT-I as well as ways to screen for comorbid sleep disorders. Ninety four (92%) of the 102 enrollees in the program completed it successfully, and 115 (63.2%) of the 182 patients who were treated completed the treatment. Of these 115 patients, 69 (60%) had moderate or marked improvement in their insomnia right after completing six sessions of CBT-I. Eighty three of the 94 (88%) people who graduated from the program were still delivering CBT-I in primary care after six to eight months.[78] These results suggest that training non-behavioral sleep medicine clinicians in CBT-I is a feasible option that can lead to positive patient outcomes; this has implications for providing access to CBT-I in remote and rural communities.

Individual components

Sleep restriction

Sleep restriction is a component of CBT-I that consolidates fragmented sleep by reducing the time allowed in bed; this leads to mild sleep deprivation and increases the homeostatic sleep drive (pressure for sleep as a function of the amount of time elapsed since the last adequate sleep episode).[79] It is the most effective component of CBT-I. In an RCT of 97 adults, a simplified version of sleep restriction, delivered over two visits with a general practitioner, was more effective than sleep hygiene recommendations alone. It significantly improved ISI (P=0.001), sleep efficiency assessed by actigraphy (P=0.006), Pittsburgh sleep quality index (PSQI) (P<0.001), and fatigue

Table 2 | Summary of the findings of the exercise studies*

Study	Type	Intervention	Outcomes	Results
Brand et al 2014[83]	Case series	Self perceived high exercise exertion	SE measured by sleep EEG 1.5 h after exercise	SE significantly improved after exercise (r=0.69; P<0.001)
Passos et al 2011[84]	Case series	Six month exercise training	Sleep parameters measured by PSG at the six month follow-up	SE significantly improved after exercise training (Cohen's d=−2.89; P<0.01), WASO (Cohen's d=1.91; P=0.04), SOL (Cohen's d=−1.67; P<0.01) Other parameters did not change
Passos et al 2010[85]	RCT	No exercise *v* moderate intensity aerobic exercise *v* high intensity aerobic exercise *v* moderate intensity resistance exercise	Sleep parameters measured by PSG the night after the exercise was completed	Only moderate intensity aerobic exercise significantly improved sleep parameters (P<0.01); SOL (ES −0.67), SE (ES 0.53), TST (ES 0.90), and WASO (ES −0.49)
Montgomery and Dennis 2002[86]	Meta-analysis (adults >60 years)	N/A	Subjective and objective measures	SOL increased by an average of 11.5 min (P=0.007) TST increased by an average of 42 min (P=0.05) PSQI scores decreased by an average of 3.4 (95% CI 1.9 to 5.4; P<0.001) Other parameters did not significantly improve
Reid et al 2010[87]	RCT (adults >55 years)	Aerobic exercise with sleep hygiene for 16 weeks *v* sleep hygiene alone	Sleep measured by PSG; sleep questionnaires	Physical activity significantly improved global PSQI scores (P≤0.0001), SOL (P=0.049), TST (P=0.04), and SE (P=0.036)

*Abbreviations: ES=effect size; N/A=not available; PSG=polysomnography; PSQI=Pittsburgh sleep quality index; SE=sleep efficiency; SOL=sleep onset latency; TST= total sleep time; WASO=wake after sleep onset.

(P=0.04) at the six month follow-up visit.[79] Sleep restriction with set bedtimes and wake times is based on the patient's previous two week sleep diary. Patients' perceptions of their own sleep quality, fatigue, and objective sleep efficiency improved with simplified sleep restriction therapy. This study suggests that simplified sleep restriction delivered in primary care may be another avenue for treating patients with insomnia who cannot complete a formal CBT-I program. Fast and effective sleep restriction can lead to manic or hypomanic symptoms in patients with bipolar disorder owing to sleep deprivation and therefore should be used with caution in these patients.[80] The same applies to patients with epilepsy because sleep deprivation can precipitate seizure activity.[81] These concerns limit the usefulness of isolated sleep restriction therapy in primary care.

Exercise

Patients are often advised that regular exercise helps improve sleep quality, and exercise is included as part of sleep hygiene. However, before 2014, patients were typically told to avoid exercise near bedtime because it was thought that this might disrupt sleep by altering the circadian rhythm, raising the core body temperature, or increasing arousal levels.[82]

In 2013, the National Sleep Foundation Sleep in America Poll assessed the timing of exercise in 1000 adults aged 23-60 years and found no difference in sleep metrics between those who exercised moderately to vigorously in the evening (≤4 hours before bedtime) and those who did not.[82] The poll did, however, find that participants who exercised vigorously in the morning had the most favorable sleep outcomes—they were more likely to report good sleep quality and less likely to report non-refreshing sleep. So, while this poll confirmed that exercise is associated with improved sleep, it contradicted previous recommendations regarding the timing of exercise in relation to sleep.

Recently, it has been shown that exercise within 1.5 hours of bedtime improves objective sleep parameters. In healthy young adults high exertion resulted in more slow wave sleep, less WASO, shorter SOL, and increased sleep efficiency.[83] Avoidance of exercise before bedtime should not be routinely recommended but patients who notice a difference in sleep quality in relation to the timing of exercise should adjust their timing of exercise accordingly.

Duration and type of exercise also play a role in the treatment of chronic insomnia. For example, moderate intensity aerobic exercise performed for 30 minutes three times a week is more effective than resistance based exercise. Again, the improvement in sleep parameters was modest at best.[84 85] Exercise as a sole intervention for insomnia is readily available and cost effective but is not universally effective. In people over 60 years, for example, exercise slightly but statistically significantly improves total sleep time, SOL, and global sleep quality but does not statistically significantly improve sleep efficiency.[86] In this age group aerobic exercise also improves overall mood and quality of life despite modest gains in sleep measures.[87]Table 2 summarizes the findings of exercise studies.

Mindfulness meditation

Mindfulness meditation is a complementary and alternative medical treatment that emphasizes awareness and attention to the present moment as a method of promoting mind-body calmness and relaxation.[88] Among the mindfulness based modalities used are a mindfulness based stress reduction (MBSR) program that teaches meditation through a structured group intervention and mindfulness based therapy for insomnia (MBTI) that incorporates MBSR into a traditional CBT-I framework.

When compared with traditional face-to-face CBT-I, MBSR was equally effective in reducing dysfunctional beliefs about sleep and in reducing ISI scores.[49 89] Compared with no treatment or sleep hygiene alone, especially in people over 75 years, MBSR improved sleep quality as measured by PSQI scores.[90-92] MBSR was also as effective as pharmacotherapy (primarily with eszopiclone 3 mg at bedtime) in improving ISI, PSQI, and other measures of insomnia outcome.[93] When compared in a randomized trial, MBTI and MBSR showed equal efficacy in subjective insomnia outcomes in the short term, but six and 12 months after therapy remission and response rates were better for MBTI.[88-96] The most recent and the highest quality RCT of mindfulness for insomnia randomized 54 adults with chronic insomnia to MBTI or MBSR or no treatment (self monitoring) for eight weeks. MBSR and MBTI improved subjective sleep parameters significantly at eight weeks, three months, and six months after treatment. The effect sizes for reduction in total wake time were 1.38 (P<0.05) and 1.05 (P=0.01) for MBTI and

MBSR, respectively. The effect sizes for a reduction in the pre-sleep arousal scale (PSAS) score were 0.88 (P<0.01) and 1.02 (P<0.01), respectively. The effect sizes for a for reduction in the ISI score were 1.57 (P<0.05) and 2.56 (P<0.01), respectively. MBTI was superior to MBSR in reducing ISI scores at three months (P<0.05) but not at six months (P=0.16). MBTI remained superior to MBSR in reducing PSAS scores throughout.[88]

Therefore, MBSR is most useful when combined with CBT-I. This may limit its usefulness in patients with severe chronic insomnia because they will face the same shortages in qualified therapists as they do when dealing with CBT-I.

A comprehensive state of the art review on mindfulness based treatments in 2014 elegantly outlined the implications and applications of mindfulness based approaches to treating insomnia. The authors pointed out that mindfulness based approaches can help target cognitive factors that are common in people with chronic insomnia. These include strategies that reduce excessive rumination and worrying, and improve selective attention and efforts to sleep. They also state that mindfulness can teach people with insomnia to observe an experience attentively and non-judgmentally, and to develop a different relationship with the experience, although they caution that this is hypothetical and more research needs to be done to verify this theory.[113]

Meditative movement (yoga and Tai Chi)

Yoga is a spiritual practice of Indian origin that incorporates movement or body positioning, breathing, and relaxation.[97] Tai Chi, which has roots in Chinese traditional medicine, also incorporates some of these elements.[97]

Some data support both Tai Chi and yoga in the treatment of insomnia but the results are generally mixed. Most studies use "no treatment" or "education" as the control and PSQI as the out outcome measure. In cancer survivors, yoga statistically significantly improved mood and reduced fatigue levels without any statistically significant impact on sleep in some RCTs,[98 99] whereas no statistically significant improvement in either subjective or objective sleep parameters was seen in others.[100 101]

Tai Chi seems to have similar effects on fatigue in cancer survivors, as seen in a RCT of Tai Chi in survivors of breast cancer.[102] The benefits of Tai Chi on fatigue are replicated in an RCT of survivors of stroke.[103] RCTs of Tai Chi reported significantly improved subjective sleep quality in patients with insomnia, those with fibromyalgia,[104] and in older people.[105-107] This significant improvement of sleep in older adults with Tai Chi is similar to that with yoga, as shown in three RCTs.[108-110] For example, yoga significantly improved both subjective sleep quality (degrees of freedom 1.63, P<0.001) and sleep duration (degrees of freedom 1.72, P<0.001) compared with no treatment.[110] Meanwhile, Tai Chi significantly improved subjective sleep quality (F=22.74; P<0.001) and sleep duration (F=16.14; P<0.001).[105]

Yoga has also been shown to be effective in treating insomnia during the menopause. An RCT randomized 44 women with menopausal insomnia to yoga, no treatment, or passive stretching. Both the yoga and the passive stretching group showed significant reductions in ISI scores and the Kupperman menopausal index (a questionnaire assessing climacteric symptoms) and an improvement in quality of life compared with no treatment (P<0.05).[111]

Another RCT compared inflammatory markers in older patients having weekly two hour sessions of CBT-I, Tai Chi, or sleep seminar education (control condition) over four months, with follow-up at seven and 16 months. Compared with the control group, CBT-I reduced systemic markers of inflammation: C reactive protein (months 4 and 16; each P<0.05), monocyte production of proinflammatory cytokines (month 2 only; P<0.05), and proinflammatory gene expression (month 4 only; P<0.01). Tai Chi significantly reduced monocyte production of proinflammatory cytokines (months 2, 4, 7, and 16; each P<0.05) and proinflammatory gene expression (month 4; P<0.001).[112]

Because of the lack of uniformity in patient populations, intervention protocols, and outcome measures, neither yoga nor Tai Chi can be recommended as a standalone alternative to CBT-I for insomnia treatment.

Self monitoring devices

It is well known that health behavior improves when it is closely monitored. Data from US consumer surveys suggest that sleep tracking devices provide an important opportunity for public health intervention. Market research reports a 500% annual growth in this market from 2011 to 2014.[114] In 2015, 10% of American adults owned a sleep tracking device.[115] Given that extending sleep typically involves the need to forgo other potentially more rewarding activities, the use of sleep tracking devices provides an opportunity to engage participants in the treatment of insomnia (K Baron, personal communication, 2015).

Research assessing the accuracy of the various commercially available devices is sparse. Compared with various clinical measures (actigraphy, polysomnography, Zmachine, single channel electroencephalography), five of the most commonly sold devices (Fitbit One, Jawbone UP, Nike+ FuelBand, GENEactiv, and LUMO Back) misreport total sleep time by 10-50 minutes and inaccurately assess arousals during the major sleep period.[116-118]

The main problem with most of these devices is that they do not provide information on their sensor accuracy or their output metric accuracy, which limits their clinical use.[119]

With more research and technological improvements these fitness tracking devices may have an important role in monitoring and managing sleep problems in patients with insomnia. Currently though patients should be discouraged from focusing solely on the device data as measures of their sleep quality (fig 2).

Advances in pharmacotherapy for insomnia

The drugs used to treat insomnia have advanced over time, but the standard formulations of the most commonly used ones can have undesired side effects. Over the past six years, three additional drugs have been added to the list of possible treatments for insomnia.

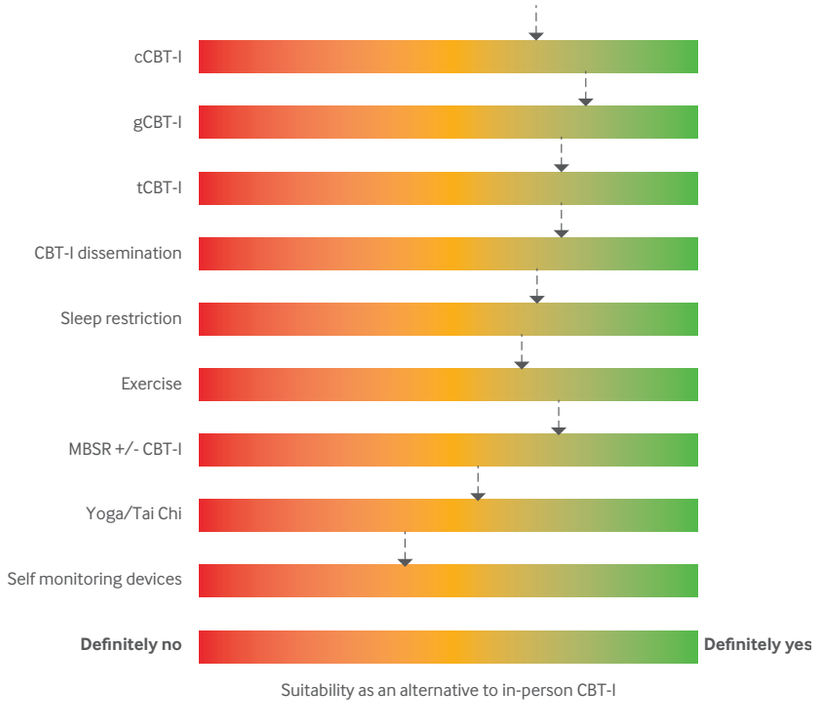

Fig 2| Comparative effectiveness of all behavioral insomnia interventions. CBT-I=cognitive behavioral therapy for insomnia; cCBT-I=computerized and online CBT-I; gCBT-I= group CBT-I; tCBT-I=CBT-I through telehealth; MBSR=mindfulness based stress reduction

Suvorexant

Mechanism of action

Suvorexant is the newest agent on the market—it is a reversible dual orexin receptor antagonist (fig 3) that was approved for use in insomnia in the US in 2014. Orexins, also known as hypocretins, are neuropeptides secreted by the lateral hypothalamus. Orexinergic neurons promote arousal in areas such as the locus coeruleus, tuberomammillary nucleus, basal forebrain, dorsal raphe nucleus, and cerebral cortex.[120] In addition, patients with narcolepsy, who have pathologic sleepiness, are deficient in orexin. There are two orexin neuropeptides, orexin-A and orexin-B,[121] and suvorexant reversibly binds to both receptors, thereby inhibiting activation of the arousal system.[122] It is thought to be effective in patients who have difficulty initiating (sleep onset insomnia) or difficulty staying asleep (sleep maintenance insomnia).

Efficacy

Multiple studies have demonstrated the efficacy of suvorexant.[120-128] In one of the earlier double blind placebo controlled trials, various doses of suvorexant were assessed.[123] Patients received a set dose of suvorexant during a four week period and placebo in another four week period. A total of 243 patients took at least one dose of suvorexant at the following doses: 10 mg (62 patients), 20 mg (61), 40 mg (59), and 80 mg (61); 228 patients completed the study. Suvorexant was more effective than placebo at improving sleep efficiency (P<0.01 for 10 mg dose at weeks 1 and 4; P<0.001 for the other three doses at weeks 1 and 4) and WASO at weeks 1 and 4 at all doses (P<0.001).[123]

A subsequent longer term randomized, placebo controlled, parallel group study over one year assessed two doses of suvorexant. Patients who met criteria for insomnia received suvorexant (40 mg if <65 years, 30 mg if >65 years) or placebo for one year. This was followed by a two month discontinuation phase during which patients taking suvorexant continued taking it or were abruptly switched to placebo, whereas patients receiving placebo continued taking placebo. The one year phase was completed by 62% (322) of the patients raking suvorexant and 63% (162) of those taking placebo. Suvorexant was more effective than placebo in improving subjective TST (38.7 min *v* 16.0 min; P<0.0001) and subjective time to sleep onset (TSO) (−18 min *v* −8.4 min; P<0.0002).[124]

A meta-analysis of four double blind randomized placebo controlled studies on the efficacy and safety of suvorexant (3076 patients) showed that 5-20 mg suvorexant (Food and Drug Administration approved doses) was superior to placebo in relation to subjective TST and subjective SOL (subjective TST: weighted mean difference (WMD)=−20.16, −25.01 to −15.30; subjective TSO: WMD=−7.62, −11.03 to −4.21).[122] However, it did not significantly reduce WASO or the number of awakenings after sleep onset.[122] The increase in TST was mainly due to increased total REM sleep, whereas benzodiazepines suppress REM sleep.[120]

Adverse effects

Suvorexant is generally well tolerated. The most common side effects are daytime somnolence, headaches, dizziness, and abnormal dreams, all of which are dose dependent.[120] The longer term placebo controlled study discussed above found that, in general, high dose suvorexant (30-40 mg) was more likely to cause adverse effects than low dose suvorexant (10 mg). However, the rate of adverse effects with 30 mg and 40 mg of suvorexant was comparable to placebo. It also found that somnolence was most common in the first three months of treatment and less common in the fourth to sixth months (suvorexant 11% to 3% *v* placebo 2% to <1%).[124]

Suvorexant is FDA approved at doses of 5-20 mg only. Higher doses have been associated with the above adverse effects as well as motor impairment, driving impairment, and unconscious night-time activity, such as sleep walking, suicidal ideation, hypnagogic hallucinations, and effects resembling mild cataplexy.[121 127] At lower doses, suvorexant has a favorable side effect profile—no rebound insomnia with abrupt discontinuation, no complex sleep related behaviors, and no withdrawal effects after four weeks, unlike many other drugs for insomnia.[120 124] However, it is unclear whether it will be as clinically effective, as indicated by the trials that used FDA approved dosages.

Cautions

Suvorexant is mainly metabolized through cytochrome P450 so blood levels of suvorexant will be higher in patients who are taking CYP3A4 inhibitors, such as azole antifungals, macrolide antibiotics, and fluvoxamine, as well as those who drink grapefruit juice.[122] Caution is therefore needed in patients taking these drugs, and the FDA has recommended that these patients are started on 5 mg rather than 10 mg.[120] Suvorexant is also contraindicated in patients with narcolepsy.

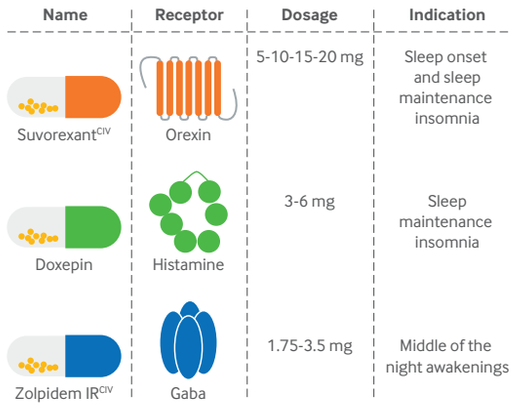

Fig 3| New Food and Drug Administration approved sleep aids

Suvorexant offers an alternative to existing insomnia drugs with a novel mechanism of action that does not seem to have the same adverse effects as existing sleep aids. However, it is important to note that suvorexant is a new drug that is not yet widely used and that the FDA approved dose (5-20 mg) is lower than the doses that were assessed in clinical trials. In the long term, we may find that it is not clinically effective at the lower doses. In addition, because it is new to the market, fewer post-market data are available and no trials have yet compared it with the other hypnotic drugs. Questions therefore remain about how suvorexant measures up against the other agents in efficacy, safety, and tolerability.

Doxepin

Although many traditional sleep aids help patients who have difficulty with falling asleep, few drugs are available for patients with sleep maintenance insomnia and early morning awakening. Longer acting drugs can help with these symptoms, but patients often have residual sleepiness in the morning. The search for a drug that targets sleep maintenance and early morning arousals is an important area because this problem occurs in more than 70% of patients with insomnia.[129]

Doxepin is a selective histamine receptor antagonist (fig 3).[130] At doses above 25 mg, doxepin has unpleasant anticholinergic and antiadrenergic side effects, but at doses of 6 mg or less its predominant mechanism of action is blockade of the wake promoting effects of histamine through histamine H_1 receptor antagonism.[130] Low dose doxepin (3 mg or 6 mg) improves sleep maintenance insomnia, and its safety and efficacy have been evaluated in a double blind placebo controlled trial in adults of all ages with chronic insomnia.[129-131] In a randomized, double blind, parallel group, placebo controlled trial, 221 patients with insomnia were randomized to 35 days of doxepin at 3 mg (n=75) or 6 mg (n=73), or to placebo (n=73); efficacy data were assessed at nights 1, 15, and 29.[129] Compared with placebo, both doses of doxepin significantly improved WASO on night 1 (P<0.0001), night 15 (3 mg: P=0.0025; 6 mg: P=0.0009), and night 29 (3 mg: P=0.0248; 6 mg: P=0.00), latency to persistent sleep (3 mg: P=0.0047; 6 mg: P=0.0007), and TST subjectively and objectively (night 1, 3 mg and 6 mg: P<0.0001; night 15, 6 mg: P=0.0035; night 29, 3 mg: P=0.0261, 6 mg: P<0.0001) without causing rebound insomnia when discontinued.

The trial also found that low dose doxepin has a favorable side effect profile with only slightly higher reports of dizziness and next day sedation compared with placebo.[129-131]

A systematic review of randomized placebo controlled trials published up to March 2014 found nine trials evaluating the safety and efficacy of low dose doxepin.[132] It found that the overall results favored the use of doxepin, with small to medium effect sizes compared with placebo for sleep maintenance (Cohen's d for polysomnographic sleep efficiency ranged from 0.41 to 0.90 for 1-6 mg doses; Cohen's d for polysomnographic WASO ranged from −0.37 to −0.76 for 1-6 mg doses) and sleep duration (Cohen's d for polysomnographic TST ranged from 0.42 to 0.90 for 1-6 mg doses), but not for sleep initiation with no significant residual next day effects.[132] On the basis of the limited data we have to date, doxepin seems to be a good alternative to other sleep aids, particularly for patients with sleep maintenance insomnia. It is well tolerated with a low side effect profile. As with suvorexant, no trials have compared doxepin with other sleep aids.

Immediate release zolpidem (sublingual zolpidem)

Zolpidem is a non-benzodiazepine receptor agonist (fig 3) that is effective in treating insomnia.[133] Both the 10 mg and 5 mg doses of sublingual zolpidem have been shown to reduce SOL more effectively than the oral zolpidem tablet.[134] However, these doses should not be taken for middle of the night awakenings because of the risk of lingering sedation in the morning.

A lower dose formulation of sublingual zolpidem has recently been studied in patients who have difficulty staying asleep. The sublingual formulation is more rapidly absorbed during the first 15-20 minutes than the regular tablet, although the total bioavailability is not altered,[135-138] and its hypnotic activity lasts for 2.5-4 hours. Compared with placebo, sublingual zolpidem 3.5 mg significantly reduces SOL and improves subjective sleep quality, as well as morning sleepiness and alertness scores.[135-138] One multicenter randomized, double blind, placebo controlled, parallel group study assessed the efficacy of sublingual zolpidem (3.5 mg) in 295 adults (median age 43 years; 68% female) with insomnia and difficulty returning to sleep after a middle of the night awakening.[135] Sublingual zolpidem significantly decreased SOL over a four week period compared with placebo (baseline 68.1 min, zolpidem 38.2 min *v* baseline 69.4 min, placebo 56.4 min; P<0.0001). In addition, patients' ratings of sleep quality (scale 1-9, with 1 being worst and 9 being best) on dosing versus non-dosing nights significantly favored the sublingual zolpidem group (zolpidem 5.71 (standard deviation 0.105); placebo 5.23 (0.107); P=0.0011). Morning sleepiness and alertness also significantly improved on the nights that zolpidem was taken (P=0.0041), but not on the nights it was not. These studies showed that sublingual zolpidem was well tolerated, with the most common adverse events being headache, nausea, and fatigue.[135-138]

Sublingual zolpidem is a therapeutic option for patients who experience a prolonged wake period during middle of the night awakenings. It should be taken only if the patient has at least four remaining hours in bed before needing to be up for the day.[139 140] As with other zolpidem formulations, the dose of sublingual zolpidem for adult women and people of both sexes over 65 years is 1.75 mg (half the standard dose approved for younger men).[137-142]

Emerging treatments

Although several drugs that regulate sleep-wake cycles rather than target the $GABA_A$ receptor are in the pipeline,[143] three $GABA_A$ receptor modulators are also being investigated.

SKP-1041

Controlled release zaleplon is designed to prevent middle of the night awakenings. A phase II study with a four way, double blind, placebo controlled, double dummy crossover design evaluated the drug at doses of 10 mg, 15 mg, and 20 mg. It found a significant reduction in time spent awake during the night.[143]

Lorediplon

A phase I study of the pharmacodynamics of lorediplon showed that it decreased WASO and increased total sleep time.[144] In a comparison with both placebo and zolpidem, lorediplon showed similar results to zolpidem. A randomized, phase II double blind, placebo controlled crossover study to evaluate the dosage needed and the drug's efficacy in sleep maintenance and sleep onset as well as its adverse effect profile began in 2014.[143]

EVT-201

The final $GABA_A$ receptor modulator, EVT-201 (1.5 mg and 2.5 mg), was assessed in a phase II, randomized, multicenter, placebo controlled study in patients aged 65-86 years for seven consecutive nights. The study showed that compared with placebo both doses significantly improved sleep maintenance (WASO −16.7 min (1.5 mg), −25.7 min (2.5 mg); both P<0.0001), sleep duration (TST 33.1 min (1.5 mg), 45 min (2.5 mg); both P<0.0001), and SOL (latency to persistent sleep (LPS) −17.0 min (1.5 mg), −20.7 min (2.5 mg); both P<0.0001). EVT-201 also improved multiple measures of subjective sleep quality, including reported TST (51.9 (1.5 mg), 51.1 min (2.5 mg); both P<0.0001), reported WASO (−29.3 min (1.5 mg), −29.6 min (2.5 mg); both P<0.0001), reported SOL (−24.0 min (1.5 mg), −25.1 min (2.5 mg); P<0.004 and P<0.0002, respectively), and reported number of awakenings (−1.1 (1.5 mg), −1.2 (2.5 mg); both P<0.0001).[143 145]

Orexin antagonists

Two orexin antagonists are also being investigated. Minerva Neurosciences is currently assessing MIN-202, a selective orexin-2 receptor antagonist. The results of the phase IIa randomized, two way crossover, placebo controlled, double blind study of MIN-202 are awaited.

In addition to MIN-202, Merck is assessing a dual orexin antagonist (filorexant; MK-6096). A phase II double blind, placebo controlled, randomized, adaptive crossover polysomnography study of 324 patients found that all doses of filorexant (2.5 mg (n=79), 5 mg (n=78), 10 mg (n=80), 20 mg (n=81)) significantly improved sleep efficiency. For example, night 1: mean change in sleep efficiency from baseline 18.3% to 25.0% with filorexant *v* 10.2% with placebo (P<0.001); week 4: mean change in sleep efficiency from baseline 16.2% to 22.4% with filorexant *v* 12.5% with placebo (P<0.004). Filorexant also improved wakefulness after persistent sleep onset (night 1: all doses, P<0.001; week 4: 2.5 mg, P=0.006, 5 mg P=0.020, 10 mg and 20 mg, P<0.001). The higher doses of filorexant (10 mg and 20 mg) were also significantly more effective in improving sleep onset insomnia (LPS: 10 mg, P<0.001, 20 mg, P=0.015) compared with placebo.[146]

Melatonin and serotonin $5HT_{1A}$ receptor agonists

The melatonin and serotonin $5HT_{1A}$ receptor agonist piromelatine and a serotonin $5\text{-}HT_{2A}$ receptor antagonist (ITI-007) are both being investigated. In phase I and phase II clinical trials, ITI-007 reportedly improved sleep maintenance in patients with insomnia and psychiatric comorbidity.[143] In a phase II, randomized, placebo controlled three arm parallel group study, piromelatine reportedly improved sleep maintenance (WASO), sleep efficiency, total sleep time, and subjective sleep duration.[143]

Although drugs are not the first line therapy for patients with insomnia, they play an important role in the clinical setting. It will be interesting to see what role, if any, these new drugs will play in the future treatment of insomnia.

Controversies over drugs for insomnia

One of the major controversies in sleep medicine for the past three years has been the potential association between the use of sedative hypnotics for insomnia and increased mortality.[147]

Insomnia has been shown to be significantly associated with mortality in men (but not women) in some countries. In a large cohort of community dwelling adult men in Finland, difficulty initiating sleep was associated with mortality (hazard ratio 2.51, 1.07 to 5.88)[148] as was the report of any insomnia symptom in a similar cohort from Norway (3.42, 1.03 to 11.35).[148]

Since the original study associating sedative hypnotic intake with mortality, several other large retrospective studies with conflicting results have been published (table 3).

Several retrospective cohort studies have also looked at zolpidem use. A daily intake of 10 mg has been associated with an increased risk of overall cancer, falls, and hip fractures both at night and during the day.[153-155] Falls at night, especially in older people with insomnia who are taking sedative hypnotics, tend to be the result of a combined effect of poor sleep quality and drugs.[159]

Cognitive impairment and risk of dementia have been reported to be as much as 50% higher with benzodiazepine use. This association remains even after controlling for depression, other chronic medical conditions, smoking, and alcohol intake.[157]

Several conclusions can be drawn from the controversy surrounding the harm caused by the use of sedative

Table 3 | Retrospective studies on mortality and the use of hypnotics for insomnia*

Study	Drugs	Morbidity risk	Mortality risk	Study limitations
Kripke et al 2012[149]	All hypnotics but mostly zolpidem or temazepam	Incident cancer: HR 1.35 (95% CI 1.18 to 1.55).	For groups prescribed 0.4-18, 18-132, and >132 doses/year, HRs (95% CI) were 3.60 (2.92 to 4.44), 4.43 (3.67 to 5.36), and 5.32 (4.50 to 6.30), respectively	Did not control for psychiatric comorbidities and did not account of mortality from insomnia
Kriegbaum et al 2014[150]	All hypnotics	Not reported	After controlling for psychiatric comorbidities, recreational substance use, and SES, the HR for all cause mortality was 1.22 (0.97 to 1.54) for intermittent users and 1.43 (1.11 to 1.85) for persistent users	Did not control for alcohol and tobacco consumption or physical activity.
Jaussent et al 2013[151]	All hypnotics	Not reported	After controlling for disturbed sleep and psychiatric and medical comorbidities, mortality risk was not significantly increased (HR 1.03, 0.84 to 1.28)For intermittent users HR was 1.11, (0.88 to 1.39)	Did not investigate morbidity, only all cause mortality
Garde et al 2013[152]	All hypnotics	Ischemic heart disease increased in men who slept <6 h/night on average and took sedative hypnotics (HR not reported)	All cause mortality was no different but risk of mortality from ischemic heart disease in short sleepers (<6 h) taking sedatives was raised (HR 3.03)	Included only middle aged men and looked only at ischemic heart disease associated mortality and not morbidity
Kao et al 2012[153]	Zolpidem	Cancer: HR 1.68 with habitual use	Not reported	Did not control for smoking, alcohol use, body mass index, or family history of cancer.
Kolla et al 2013[154]	Zolpidem	Inpatient falls: HR 6.39	Not reported	Not community dwelling people
Bakken et al 2014[155]	All hypnotics but mostly zaleplon, zopiclone, or zolpidem	Hip fractures: standardized incidence ratio 1.3	Not reported	Only nursing home population
Taipale et al 2009[156]	All sedating drugs	Not reported	No increased mortality risk HR 1.01	Included all sedating drugs, not only hypnotics
Billioti de Gage et al 2012[157]	Benzodiazepines	Dementia: HR 1.6	Not reported	Did not control for the diagnosis for which benzodiazepine was prescribed
Chen et al 2013[158]	All hypnotics	Not reported	In people over 65 years risk of mortality was increased (depending on number of hours of sleep/night, HR ranged from 1.37 (1.09 to 1.73) to 1.66 (1.28 to 2.17)	Did not control for sleep disorders, and sleep data were all subjective

*Abbreviations: CI=confidence interval; HR=hazard ratio; SES=socioeconomic status.

hypnotics and the limitations of the underlying evidence. Firstly, adverse effects from taking sedative hypnotics for insomnia are not as alarming as these studies initially suggested. However, these drugs are not as benign as previously thought. Secondly, CBT in its many guises should be the first line treatment for insomnia. Thirdly, sedative hypnotics should be prescribed for short periods and in specific situations, and their use should be even more limited in people over 65 years.

Guidelines

The American Academy of Sleep Medicine has not published specific guidelines for the treatment of chronic insomnia since 2006, when it assessed the various behavioral interventions but not the pharmacotherapy options.[160] In 2010, the British Association for Psychopharmacology published a consensus statement with the participation of experts from mainland Europe and North America. It recommended that CBT-I and related non-pharmacologic methods should be first line treatments for chronic insomnia and that efforts should be made to increase their availability. Pharmacologic treatments should not be first line, but if necessary they should be used with caution, intermittently at first, and their use should be reassessed every three to six months.[161]

Conclusions

Several advances have been made in the management of chronic insomnia over the past decade. In addition to increased recognition of the seriousness of this condition, the various morbidities associated with it, and the higher risk of mortality that it confers, there has been a concerted effort to develop ways to deliver safer and effective treatments to a wider patient population.

CBT-I remains the most effective treatment, and ways to disseminate it beyond the small number of certified and trained practitioners have been developed. These include cCBT-I, tCBT-I, gCBT-I, and intense short term training of non-sleep specialists to deliver basic CBT-I to larger groups of patients with insomnia. Other non-pharmacologic methods that may be promising include exercise, sleep restriction, meditative movement, and MBSR. These alone or combined with elements of CBT-I can be useful in certain groups of patients. Self monitoring devices are promising but are currently not well enough developed to have a major impact on the management of insomnia. In the pharmacologic arena, suvorexant blocks orexin receptors, a novel target for reducing wakefulness and enhancing sleep. Low dose doxepin is an antihistamine that has a favorable efficacy and safety profile. Low dose and immediate release zolpidem has been shown to be effective for middle of the night insomnia without the next day sedation of regular zolpidem. A few other drugs in the pipeline also seem to be promising for the treatment of chronic insomnia. The controversy surrounding the safety of chronic use of sedative hypnotics should not mean that patients with chronic insomnia are left without adequate treatment. However, drugs should be prescribed with caution, preferably for the short term only.

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