Integrative Medicine for Insomnia

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KEYWORDS

• Sleep disorders • Insomnia • Integrative medicine • Alternative therapy
• Complementary medicine

KEY POINTS

- Insomnia is a common sleep disorder that is associated with poorer physical and psychological health.
- The comprehensive evaluation of a patient's health status is important when diagnosing insomnia and devising a treatment plan.
- Consistent evidence has demonstrated the efficacy of cognitive-behavioral therapy (CBT) for insomnia. CBT should be considered as first-line treatment.
- There is a growing body of literature suggesting that mindfulness-based stress management, yoga, and tai chi may improve insomnia symptoms. Current data do not support routine use of dietary supplements for sleep.
- Well-designed research studies are needed to better understand the impact of other complementary treatment approaches for insomnia (eg, acupuncture).

INSOMNIA

Insomnia is characterized by difficulty initiating and/or maintaining sleep or early morning awakenings. It is a remarkably common problem across the life span. One-third of the general population experiences insomnia symptoms and 10% to 15% meet criteria for insomnia disorder. Insomnia disorder is marked by chronic sleep disturbance that causes distress or impairs daytime function. Insomnia imparts tremendous societal and economic impact, resulting from workplace absenteeism, accidents, and declines in productivity.[1–3] Chronic sleep dysfunction is also associated with a variety of deleterious health outcomes, such as cardiovascular disease,[4,5] diabetes,[6] and obesity,[7] as well as impaired mood and cognitive function.[8,9]

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Despite the psychological, physical, and financial burden of insomnia, it remains an underdiagnosed and poorly understood condition. In both primary care and the hospital setting, insomnia is often inadequately discussed and actively treated.[10,11] There is a notable gap between clinical practice guidelines for evaluating and treating chronic insomnia and current clinical care. Given this gap, patients commonly self-treat with alcohol[12] or nonprescription sleep aids, with nearly 20% using either a prescribed and/or a nonprescribed sleep aid within the past month.[13] Those who do consult their physicians about their poor sleep are often treated with pharmacotherapy.[14] At least 6 million Americans (3.0%–3.5% of the population) report use of a prescription medication for insomnia within the past 30 days.[13,15] Rates of use have increased over the past decade.[13] There are concerns regarding the use of pharmacotherapy as insomnia treatment, including dependence,[16] increased risk for motor vehicle accidents,[17] falls in the elderly,[18] and psychiatric and medical conditions.[19,20] Moreover, there are limited data on long-term efficacy.[21] Given these concerns and patient preferences often for nonpharmacological treatment,[22] it is important for patients with insomnia to be offered evidence-based nonpharmacologic approaches that may improve their sleep. Integrative insomnia therapies, including complementary and alternative medicine (CAM), are treatment options that are commonly used by adults with insomnia in the United States.[23–25] Biologically based therapies (eg, herbs) and mind-body therapies (eg, meditation) are the most commonly used CAM therapies for insomnia.[24]

INSOMNIA EVALUATION

Providers should remember that insomnia symptoms are likely underreported during routine clinical care. Patients often overlook their poor sleep because they may misattribute it as a symptom of another health issue. They also may have become resigned to the condition or are not aware that effective treatment options exist.[26–28] The evaluation of insomnia requires a broad approach and starts with a thorough medical and psychiatric history. Several risk factors exist for insomnia that should alert clinicians to the increased possibility of insomnia disorder (**Box 1**).[9,29–32]

Patients should be specifically asked about the timing of their sleep habits (eg, when they go to sleep; how long it takes them to fall asleep; frequency and duration of night awakenings; wake time; naps; quality and variability of their sleep pattern). Further, the

Box 1
Risk factors for insomnia

- Female sex
- Older age (>60 years)
- Medication side effects
- Night/Rotating shift work
- Travel across time zones
- Psychosocial distress
- Substance use
- Pregnancy
- Poor physical health (eg, congestive heart failure, sleep-disordered breathing)
- Poor mental health (eg, depression, anxiety, schizophrenia)

provider should discuss psychological (eg, depression) and physiologic (eg, medication use, chronic pain) factors that may be directly impacting sleep. The review of systems should inquire about symptoms consistent with of other sleep disorders, such as sleep apnea and restless legs syndrome. In addition, understanding behaviors (eg, using electronic devices in bed, staying in bed when not sleeping, stress-relieving practices including exercise), occupational factors (eg, shift work), and environmental disruptors (eg, frequent time zone travel) are important. Both prescription and nonprescription medications, as well as "drugs of habit" (eg, alcohol and caffeine) should be reviewed. Last, assessment of the daytime consequences of insomnia is critical, as these may be the main outcomes that treatment targets.

Given the known variability in sleep patterns, the collection of daily sleep diaries or logs for several weeks is a critical tool in the evaluation of insomnia. In addition to providing information on sleep timing, patterns often become evident that suggest circadian rhythm disorders or other important behaviors, such as excessive time in bed not sleeping. Data supporting the validity of commercially marketed wearable devices for assessing sleep are limited and are therefore generally not recommended.[33] For patients who are unable or unwilling to keep a sleep log, actigraphy[34] (a validated device worn on the wrist) may be used to track sleep/wake activity. However, these are generally limited to the sleep specialty clinic or research setting. Polysomnography (ie, sleep study) is not routinely indicated for the evaluation of insomnia unless there is concern for other sleep disorders (eg, obstructive sleep apnea).[35]

Should insufficient information be obtained during the clinical interview or sleep logs, there are additional instruments that can be used to gain further insight on sleep-related information. Providers should consider the use of standardized measures collected before or during a medical visit. Brief measures that can be considered include the Insomnia Severity Index[36] and Pittsburgh Sleep Quality Index (PSQI).[37] These measures require relatively minimal patient burden, provide a clinician with information to initiate a conversation with the patient, and quantify changes in symptoms over time.

In the primary care setting, patients may present with subclinical levels of insomnia symptomatology. In these cases, a stepped care approach can be used whereby increasing levels of patient need and distress warrant referrals to increasing levels of specialty sleep care and resources.[38]

TREATMENT OF INSOMNIA

Positive patient outcomes may come in the form of subjective improvements to nighttime (eg, improved overall sleep quality) and/or daytime functioning (eg, less fatigue and improved concentration). Objective improvements to sleep-specific variables may include decreased sleep-onset latency, less wake after sleep onset, and improved sleep efficiency. These variables describe common challenges experienced by patients with insomnia. Specifically, sleep-onset latency refers to the time taken for a patient to fall asleep. Wake after sleep onset describes the total amount of time a patient spends awake in the middle of the night. Sleep efficiency describes the ratio of the total time spent asleep divided by the total sleep opportunity.

Integrative Therapies

Cognitive-behavioral therapy

Cognitive-behavioral therapy for insomnia (CBT-Insomnia) is composed of several primary components: sleep restriction, stimulus control, cognitive restructuring,

sleep hygiene, relaxation, and relapse prevention. Sleep restriction[39] limits time in bed to increase sleep drive and regulate circadian rhythms. Stimulus control[40,41] provides patients with "rules" to retrain their minds and bodies to relearn to associate sleep with their bed and bedroom environment. Stimulus control also aims to reduce anxiety and/or conditioned arousal that individuals experience when attempting to fall asleep. Cognitive restructuring attempts to address, challenge, and reshape the negative beliefs and distorted cognitive patterns about sleep and sleep loss that further perpetuate chronic sleep difficulties. For example, patients may worry that they may not be able to function at work the next day if they are not able to fall asleep quickly enough. This can then further increase their anxiety at bedtime, creating a vicious cycle making it more difficult to fall asleep. Sleep hygiene focuses on education about factors that promote sleep and discourage behaviors that are detrimental to sleep (eg, avoiding nicotine, caffeine, and alcohol before bedtime).[42] It is noted that sleep hygiene recommendations are often provided as monotherapy, and evidence indicates that may not be an effective treatment, by itself, for insomnia disorder.[43] Relaxation therapy can incorporate various techniques, all with the goal to reduce disruptive physical and/or cognitive arousal at bedtime. A considerable body of literature supports multiple forms of relaxation for insomnia, including progressive muscle relaxation, imagery, and autogenic training.[39–41,44–46] Relapse prevention strategies integrate the behavioral, cognitive, and educational elements, promote adherence, help the patient identify high-risk situations, and incorporate steps to reduce relapse. Effective individual components of CBT-Insomnia (sleep restriction and stimulus control) can be demanding for a patient and often create a short-term exacerbation of sleep problems.[47] Consequently, adherence may be poor[48] and may explain why some patients continue to experience insomnia symptoms after treatment.[49]

Numerous randomized controlled trials (RCTs) have demonstrated that CBT-Insomnia is highly effective.[50–52] A meta-analysis of 20 RCTs showed that CBT-Insomnia effectively improves multiple sleep outcomes (eg, wake after sleep onset, sleep efficiency).[53] Direct comparisons between CBT-Insomnia and pharmacologic treatments indicate that CBT-Insomnia is equivalently efficacious, with the benefits of CBT-Insomnia maintained over a longer duration.[16,49,52,54] In addition, CBT-Insomnia also may improve outcomes for depression, anxiety, and quality of life.[55,56] CBT-Insomnia is also efficacious in multiple patient subpopulations, such cancer,[57,58] chronic pain,[59] and numerous additional comorbid medical and psychiatric disorders.[60] Given the preponderance of evidence supporting its efficacy, several professional organizations consider CBT-Insomnia as first-line therapy for insomnia.[61–63]

Barriers to treatment with CBT-Insomnia exist even when a patient is aware and motivated to change his or her behavior. One major limitation is that there are relatively few trained providers to deliver this intervention. There are estimated to be fewer than 700 behavioral sleep medicine experts in the United States,[64] mainly limited to major cities.[65] Further, CBT-Insomnia is time and resource intensive, as it was developed to be provided over 6 to 8 individual, in-person sessions.[66] This can be a prohibitive duration due to travel time to and from the provider and out-of-pocket expenses for the patient. To combat these barriers, there are ongoing efforts to train nonsleep specialists[67] to deliver CBT-Insomnia treatment via group and telehealth mechanisms.[68–72] Briefer programs are also in development.[73] Evidence is promising that these novel delivery approaches can effectively improve insomnia symptoms. Finally, it is noted that CBT-Insomnia research has been primarily conducted in adults, with different approaches required for pediatric populations.[53,74]

Mindfulness-based practices

The use of mindfulness-based practices to improve insomnia symptoms has garnered recent interest, specifically mindfulness-based stress reduction.[75,76] Mindfulness practices purposefully bring awareness to the present moment by directing attention to the breath, physical sensations, feelings and/or thoughts. These practices aspire to view the moment with a mindset that is accepting, patient, and kind.[77] Although no definitive mechanisms have been established to explain how mindfulness-based practices affect sleep, several reasonable interrelated hypotheses have been suggested. One theory postulates that mindfulness-based practices may act through the reduction of cognitive and physiologic hyperarousal,[78] which has been implicated as a contributor to the development and/or maintenance of sleep problems.[79] This explanation posits that during the day, individuals engage in functional information processing, such as making decisions or solving problems. In the evening, these processes should deactivate and therefore facilitate sleep. A mindfulness-based practice potentially allows cognitive and physiologic deactivation and a reduction in hyperarousal by encouraging the practitioner to accept and "let go" of their daily concerns. A second hypothesis is based on literature suggesting people who ruminate tend to sleep worse.[80,81] Mindfulness-based practices may facilitate sleep by helping individuals ruminate less.[82] Recent evidence supports this notion that mindfulness-based practices reduce repetitive negative thinking, which in turn improves psychological outcomes.[83] Finally, it has been suggested that mindfulness-based practices may help individuals better pay attention to the present moment, thereby reducing the focus on not being able to sleep and/or the consequences of poor sleep.[84,85]

Within the past several years, multiple efforts have been taken to advance the science evaluating mindfulness-based practices as a treatment for insomnia. Researchers have delivered mindfulness-based practices to the general adult and cancer populations, with significant improvements to sleep in general. Although sample sizes were relatively small in some studies, evidence suggests that a mindfulness-based intervention can improve insomnia symptoms (eg, reduce total wake time, improve sleep quality) in those with both insomnia symptoms and insomnia disorder,[86–88] with efficacy comparable to that of hypnotic medications.[89] When compared with CBT-Insomnia, a mindfulness-based approach developed for cancer populations was effective at improving insomnia symptoms, but inferior to CBT-Insomnia on some sleep outcomes.[90] Other efforts have used mindfulness training as adjunctive treatment to CBT-Insomnia, creating a hybrid approach.[91] Findings have been mixed with respect to whether adding mindfulness-based practices to CBT-Insomnia improves insomnia more than CBT-Insomnia alone.[92,93]

To date, mindfulness-based practices in the treatment of insomnia show potential, and should be considered as a possible second-line or adjunctive therapy to other therapeutic approaches with a stronger evidence base (eg, CBT-Insomnia). Mindfulness-based approaches may play a particularly key role in insomnia treatment for 3 categories of patients: (1) interested in acceptance and commitment-based treatments designed to increase cognitive flexibility; (2) failed or would prefer not to attempt CBT-Insomnia, and (3) have medical/psychological conditions that may be exacerbated by CBT-Insomnia (eg, bipolar disorder). Future work is important before mindfulness-based treatment of insomnia can be considered for routine integration into clinical care. Mechanistic studies, standardized mindfulness-based insomnia protocols, and trials directly comparing mindfulness-based practices with CBT-Insomnia and pharmacologic therapies are needed.

Mind-body movement practices (yoga and tai chi)

Both yoga and tai chi represent multicomponent interventions that are thought to evoke similar physiologic processes to traditional relaxation training. Both have been investigated as treatments for insomnia. Yoga is a popular mind-body practice originally derived from India. Mechanistically, yoga acutely impacts autonomic nervous system activity and may reduce gamma-aminobutyric acid (GABA) levels and inflammatory markers over time.[94,95] These are plausible neurobiological pathways by which yoga may improve sleep quality and duration. Data from small RCTs suggest yoga improves subjective[96–99] and objective[99,100] sleep quality, and reduces insomnia symptoms in adults with chronic medical conditions.[96,98,101–104] One of the largest RCTs of yoga demonstrated reduced hypnotic medication use in cancer survivors with sleep disturbance by 21% in the yoga group compared with 5% in the control group.[99] Although clinically meaningful differences in self-reported sleep quality were seen, improvements to daytime function were more modest. Few studies have evaluated yoga specifically for insomnia disorder. One of the first studies to explore yoga in patients meeting standard diagnostic criteria for insomnia was a single-arm 8-week trial exploring Kundalini yoga, a style that emphasizes breathing techniques and meditation. Among the 20 participants completing the study (of 34 entering treatment), improvements were seen in diary-reported total sleep time, sleep quality, sleep efficiency, and total wake time.[104] Another pilot RCT reported that postmenopausal women with insomnia disorder experienced a greater reduction in insomnia symptom scores with yoga compared with a control, but without differences in polysomnographic outcomes. Another small, single-arm study exploring a combination of Hatha and viniyoga for sleep difficulties in patients with osteoarthritis found reductions in insomnia symptom scores and improvements in reported sleep-onset latency and sleep efficiency. No changes were seen in actigraphy outcomes, however.[101] To date, although the emerging data on yoga are encouraging, many clinical studies have studied participants experiencing a general sleep disturbance, rather than insomnia disorder. Furthermore, yoga studies measuring sleep outcomes have suffered from common methodological limitations, such as small sample sizes, lack of clearly defined protocols, and limited use of objective outcome measures.

Similar to yoga research, there is an emerging body of work on tai chi for sleep disturbance that has focused more on sleep quality (ie, change in self-report measures such as the PSQI) rather than insomnia disorder. Several RCTs of tai chi for sleep have demonstrated improvement in reported sleep quality, particularly among older adults. Irwin and colleagues[105] demonstrated that older adults with moderate sleep complaints who practiced tai chi were more likely to achieve significant improvements in sleep quality compared with those receiving health education (63% vs 32%, respectively). Other tai chi studies evaluating sleep quality as the primary outcome found similar improvements for older adults compared with a low-impact exercise group.[106] Another study found a clinically meaningful improvement with tai chi compared with a waitlist control.[107] Similar improvements in sleep quality have been found in patients with fibromyalgia.[108,109] However, small studies in other clinical populations, such as breast cancer[110] and arthritis,[111] have not demonstrated positive results. A recent comparative effectiveness study indicated that tai chi was less effective than CBT-Insomnia for chronic insomnia disorder, but more effective in improving sleep quality than education on aging and sleep.[112] Therefore, tai chi may improve sleep quality in diverse patient populations, and in particular older adults. Its impact on objective measures of sleep as well as chronic insomnia disorder needs to be further elucidated.

Acupuncture

A Cochrane review conducted in 2009 indicated that definitive conclusions cannot be made on acupuncture's efficacy for insomnia.[113] This conclusion was reached due to the limited number of RCTs and limited sample sizes. Further, existing research is hampered by design limitations. For example, publications have provided limited information about inclusion/exclusion criteria, randomization procedures, outcomes measured, missing baseline data, and the specific acupuncture approach(es) used.[114,115] Future research efforts should improve methodological rigor to assess whether acupuncture therapy for insomnia can be recommended.

Dietary supplements

Valerian Valerian (*Valeriana officinalis*) has been one of the most rigorously evaluated supplements for sleep purposes. Valerian's effects on the central nervous system have been attributed to valepotriates, valerenic acid, and other constituents in the essential oil.[116] Valerian extracts do contain small amounts of GABA, a key sleep-promoting neurotransmitter. However, whether exogenous GABA can cross the blood-brain barrier to produce sedative effects is not known.[117] Although numerous case series and RCTs in adults have suggested valerian impacts sleep, the totality of evidence supports generally weak effects on sleep, and minimal benefit for patients with insomnia disorder. A recent meta-analysis included only studies evaluating insomnia disorder (14 RCTs, n = 1602),[118] defined by established diagnostic criteria, standardized instruments, or medical diagnosis. This study found no difference in short-term ($\leq$6 weeks) sleep outcomes between valerian and placebo. It is important to note that a wide range of dosages and preparations were tested, and the risk of bias could not be adequately assessed given the general lack of information on preparation methodology. The rate of adverse events was similar between valerian and placebo. Given these limited data on harms, and limited evidence supporting clinically meaningful change in outcomes, the American Academy of Sleep Medicine (AASM) guides practitioners to not recommend valerian for insomnia disorder.[73]

Melatonin Melatonin (N-acetyl-5-methoxytryptamine) is a hormone synthesized from tryptophan and secreted in the pineal gland. Current evidence in humans supports melatonin's roles as a chronobiotic, influencing circadian timing, and as a modest somnogen, initiating and maintaining sleep. As light is the most important environmental cue modulating endogenous melatonin release, melatonin levels peak in darkness and are low during the daytime. In the United States, exogenous melatonin is a popular over-the-counter dietary supplement recommended for disorders of the sleep cycle, such as shift work and jet lag. In Europe, it is available only by prescription. In general, data supporting exogenous melatonin for insomnia are weak. A meta-analysis included 19 melatonin trials with 1683 patients with "sleep disorders" (ie, insomnia [n = 14], delayed sleep phase syndrome [n = 4], and rapid-eye movement behavior disorder [n = 1]). Compared with placebo, melatonin reduced sleep-onset latency by about 7 minutes, prolonged subjective (but not objective) total sleep time by approximately 8 minutes, and had modest effects on sleep quality.[38] A clinical guideline put forth by the AASM suggested against the use of melatonin for treatment of sleep onset or sleep maintenance insomnia.[73]

In contrast, the AASM recommends timed oral administration of melatonin for delayed sleep-wake phase disorder in adults and children. Delayed sleep-wake phase disorder can present as sleep-onset insomnia. This disorder is most apparent when the patient's biological clock is misaligned with his or her time zone. This often results in difficulty falling asleep "when needed" and awakening at a desired time earlier than

the biological wake time. This commonly leads to insufficient sleep and reports of insomnia symptoms.

In general, melatonin is well tolerated in adults with few reported adverse events in a dose range of 0.1 mg to 10 mg.[119] Caution in children/adolescents and women of reproductive age should be exercised due to limited long-term studies and potential hormonal effects.[119] Melatonin should generally not be used during daytime due to sedation. In a placebo-controlled trial, oral melatonin decreased coagulation activity within 1 hour of dosing in healthy men. Therefore caution should be used with anticoagulants.[73]

One major issue with melatonin, and other over-the-counter dietary supplements, is the relative lack of standardization and regulation. A recent study of 31 melatonin products available in Canada found that the melatonin levels in the pills ranged between 83% and 478% of the melatonin dose reported on the label. More than 70% of the products varied from the labeled dose by more than 10%. There was also lot-to-lot variability among manufacturers. Furthermore, 26% of products also contained serotonin.[113] Therefore, if melatonin is recommended in the short term for insomnia symptoms in adults, or for treatment of circadian rhythm disorders, only products that have been third-party verified (eg, US Pharmacopeial Convention) should be used.

Other supplements The data examining other dietary supplements for insomnia are sparse. German chamomile (*Matricaria recutita*) has been used for sleep for thousands of years.[120,121] Common preparations include tea (3 cups per day) or in tinctures (1–4 mL/d). Preclinical studies suggest chamomile's mechanism of action is due to the flavone, apigenin, which modulates GABA receptors.[122] Chamomile has been studied in a few short-term trials. The most rigorous study, conducted in 34 patients, examined high-grade extract chamomile (270 mg, twice a day) for primary insomnia. Modest benefits were reported for some sleep outcomes, although conclusions were limited by small sample size.[123] Chamomile is in the same plant family (Asteraceae) as ragweed, and therefore chamomile should be used with caution in patients with a history of hay fever, as allergic reactions, including rare cases of anaphylaxis, have been reported.[120] Given chamomile's relatively safe profile, it may be reasonable to use chamomile for insomnia symptoms based on patient preference and values, although rigorous evidence supporting its efficacy is generally weak.

Exogenous consumption of the amino acid L-tryptophan has also been purported to induce sleep, although data are limited. One short-term study suggested that 250 mg tryptophan resulted in significant improvement in subjective and objective measures of sleep in persons without insomnia.[124] Another small study suggested improved sleep with L-tryptophan in sleep in individuals undergoing drug detoxification.[108] Two other short-term studies suggested modest reductions in sleep-onset latency in chronic insomnia at differing dosages. Based on available evidence suggesting clinically meaningful improvements, the AASM recommends against use of L-tryptophan for chronic insomnia.[73] It should be noted that in the 1990s, L-tryptophan was recalled from the market due to safety concerns, as it was linked to more than 1500 reports of eosinophilia-myalgia syndrome.

Lavender, specifically English lavender (*Lavandula angustifolia*), usually in the form of oil or tea, has been used for sleep purposes. Several small, very short-term (<1 week) studies in healthy individuals suggest that lavender oil may improve sleep quality.[125] In recommended doses, lavender is generally considered to be well tolerated in adults,[126] although a case report of pre-pubertal gynecomastia after use of lavender and tea tree oils has been reported.[127]

SUMMARY

Insomnia symptoms and chronic insomnia disorder are very common and frequently present in the general health care setting. There is high-quality evidence for use of CBT as a primary treatment for insomnia, with emerging evidence supporting use of additional mind-body therapies, such as mindfulness meditation. Tai chi and yoga also may improve sleep quality, particularly among older adults. However, their role in treating chronic insomnia disorder is unclear. Although dietary supplements are commonly used for insomnia, the totality of data does not currently support routine use for most patients with sleep disturbance. The role of other therapies, such as acupuncture, in treating insomnia remains uncertain. Patients with insomnia do not commonly discuss their use of complementary therapies with providers. It is essential that the patient's use of such therapeutic approaches is fully assessed.

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