The State of Insomnia and Emerging Trends

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Abstract

Recent research into the pathophysiology of insomnia has brought a shift in the approach to treatment. Insomnia rarely occurs in isolation and is typically comorbid with other conditions. Rather than simply treating the primary disorder, whereby symptoms of insomnia may go unaddressed, now there is a push to acknowledge the existence of chronic insomnia as a disorder that itself merits treatment. This recognition is due to the identification of pathophysiologic changes and associated morbidity, which can be substantial. Insomnia patients have increased risk for psychiatric disorders, especially depression, anxiety, decreased quality of life, increased healthcare utilization and costs, drug/alcohol abuse, decreased occupational performance, and increased falls/accidents. Current management patterns explore non-nightly or discontinuous hypnotic treatment—non-nightly flexible, non-nightly semiflexible, non-nightly fixed, and flexible timing—which deviates from past trends of continuous dosing with hypnotics. These trends reflect a change from considering insomnia a symptom to treating insomnia as a disorder.

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Recent research into the pathophysiology of chronic insomnia has brought about a shift in the management of insomnia. The National Institutes of Health issued a statement in 2005 regarding the nature and management of chronic insomnia based on the findings of an independent panel of sleep experts. The panel weighed all evidence available to date on insomnia and prepared a State-of-the-Science Conference Statement, the first consensus statement to be issued on insomnia since 1983. The consensus statement reflects the evolving trend of considering insomnia as a disorder and not merely a symptom, as was the accepted view in the 1980s. Also, insomnia rarely occurs in isolation, but rather is typically comorbid with other conditions. The 2005 statement also reflects the change in approach to treatment. Rather than simply treating the primary disorder, whereby symptoms of insomnia may go unaddressed, now there is a push to acknowledge the existence of chronic insomnia as a disorder that itself merits treatment. Substantiation that insomnia is a disorder is based on data that insomnia is associated with pathophysiologic changes and results in morbidity, as is evidenced by impairment in function and quality of life (QOL).[1]

Insomnia encompasses 1 or more of the following: difficulty initiating sleep; difficulty maintaining sleep; waking up too early; and/or sleep that is chronically nonrestorative or of poor quality.[2] The determining factor in relating these symptoms to insomnia is that the sleep difficulty occurs despite adequate opportunity and circumstances for sleep. In addition to the reported difficulties with sleep, the diagnosis of insomnia also includes reports of daytime impairment or distress related to the nighttime sleep difficulty. These impairments may include, but are not limited to, problems such as fatigue, memory impairment, mood disturbances, proneness for errors, tension headaches, and gastrointestinal symptoms in response to sleep loss.[3] The recognition of insomnia as a disorder is due to the identification of pathophysiologic changes and morbidity associated with it. This article will discuss the pathophysiology and the morbidity associated with insomnia and provide insight into the emerging trends for the management of insomnia.

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Pathophysiology of Insomnia

Insomnia can present as an isolated disorder or as a condition that coexists with medical and psychiatric disorders. Chronic primary insomnia can be characterized as a patient being in a state of hyperarousal, manifesting in problems such as excessive worry and physiologic hyperactivity.[4] Evidence to support hyperarousal includes physiologic changes such as increased levels of catecholamines,[5] increased basal metabolic rate,[6] increased body temperature,[7] altered heart rate,[6] increased level of central nervous system (CNS) metabolic rate,[8] and elevated electroencephalograph activity.[9,10] The pathophysiology of hyperarousal in insomnia has been postulated to be related, in part, to increased corticotropin-releasing factor (CRF) activity. This hypothesis is supported by the clinical and neuroendocrine similarities between insomnia and major depressive disorder (MDD), abnormal CRF regulation in major depression, and findings demonstrating the relationship between hyperactivity of CRF neurons and clinical features of insomnia, which include hyperarousal and sleep disturbances.[11] Data also exist to suggest that the hypothalamic-pituitary-adrenal (HPA) axis is overactive in patients with insomnia. The HPA axis is involved in the secretion of CRF which, in turn, acts on receptors in the anterior pituitary to cause a release of adrenocorticotropic hormone (ACTH) into the bloodstream. The ACTH then acts on the adrenal cortex to cause the production and release of cortisol.[12] Patients with chronic insomnia have been shown to have significantly higher levels of ACTH and cortisol than individuals without insomnia. The findings further demonstrate that insomnia is, indeed, a disorder of CNS hyperarousal.[13]

In addition to the sleep-wake system affected by being in a state of hyperarousal, other systems and disorders are likely to be affected. Mood, anxiety levels, and pain thresholds may also be affected by psychologic and physiologic changes observed with being in a state of arousal. A possible link between stress, insomnia, depression, and other comorbidities includes decreased immune function and increased proinflammatory activity. Increased secretion of proinflammatory cytokines has been observed in normal sleepers experiencing sleep deprivation.[14] It is important to recognize that these are data in sleep deprivation and, thus, confirmatory data in insomnia are needed. Research is ongoing regarding the pathophysiology of insomnia, with each step providing more insight into the disorder.

Morbidity of Insomnia

The effects of insomnia on patients can result in a substantial amount of morbidity for those suffering from insomnia. Patients with insomnia have a demonstrated increased risk for psychiatric disorders especially depression, decreased QOL, increased healthcare utilization and costs, absenteeism and decreased occupational performance, and an increase in falls and/or accidents.

An association between insomnia and psychiatric disorders such as depression, anxiety, alcohol abuse, and drug abuse has been demonstrated. Multiple published studies have shown insomnia to be a risk factor for MDD. Odds ratios for the studies range from a relative risk of 2 to 10 for the increased likelihood of MDD given a patient has insomnia.

Effects of insomnia on QOL have proven difficult to measure. Health-related QOL (HRQOL) is defined as the "overall state of well-being that individuals experience as assessed by subjective and objective measures of functioning, health, and satisfaction with the important dimensions of their lives."[15] Measuring HRQOL in patients with insomnia is problematic due to the unstandardized morbidity measures surrounding the disorder. Several questionnaires and/or measurement tools do exist that provide information regarding insomnia and other sleep disorders.[15] Work done in the area of insomnia and HRQOL has found insomnia to be independently associated with HRQOL across multiple domains, including mental health, vitality, and general health perceptions, as documented in a study by Katz and McHorney.[16] The study also determined that HRQOL in patients with insomnia was worsened to almost the same extent as HRQOL in patients with chronic conditions such as congestive heart failure and depression. A study conducted by Hatoum et al surveyed patients across 5 managed care organizations on HRQOL.[17] Results showed patients with insomnia had lower HRQOL scores based on the 36-Item Short Form Health Survey (SF-36) measurement tool. Insomnia was consistently significantly associated with worsened outcomes across all domains of the SF-36 measurement tool.

In addition to worsened HRQOL, patients with insomnia have historically experienced increased healthcare utilization compared with patients who did not suffer from insomnia. Healthcare utilization encompassed prescription and nonprescription medications, physician visits and calls, laboratory work, emergency department visits, and hospitalizations. The study by Hatoum et al concluded that the severity of insomnia played a role, as patients with more severe cases of insomnia (classified as Level II) reported higher healthcare utilization than Level I insomnia patients.[17] An analysis of pharmacy and medical claims data by Ozminkowski et al found average direct and indirect costs for younger adults to be approximately $1200 higher per insomnia patient when evaluating costs in the 6 months before the onset of insomnia compared with 6 months of costs in matched patients without insomnia.[18] Analysis of direct costs in elderly patients with insomnia yielded costs approximately $1100 higher per patient than those patients without insomnia.

Further contributing to the indirect costs of insomnia is its effect on productivity, particularly in the workplace. Insomnia negatively affects work productivity, as absenteeism is associated with insomnia. Insomnia patients averaged 15.8 days absent from work per year compared with 1.6 days absent in a control group in a study conducted by Zammit et al.[19] Similarly, patients with a sleep problem had a higher percentage rate of missing work than patients with no sleep problem.[20]

The morbidity of insomnia can be substantial, affecting all aspects of a patient's life. Recognizing the effects of insomnia is essential for the treatment and management of chronic insomnia.

Emerging Trends in Insomnia Management

Nonpharmacologic treatments for the management of insomnia include behavioral and cognitive techniques that focus on modifying factors affecting sleep difficulties. These strategies include a focus on sleep hygiene, education, relaxation, stimulus control, and sleep restriction. Pharmacologic therapies for treating insomnia have previously focused on benzodiazepine receptor agonists. Current management patterns are exploring the effectiveness of non-nightly or discontinuous hypnotic treatment. This approach to treatment may offer the benefits of relief from insomnia while preventing the nightly use of medications.[21] Strategies for non-nightly dosing include non-nightly flexible, non-nightly semiflexible, non-nightly fixed, and flexible timing. Non-nightly flexible dosing allows patients to treat themselves on an as-needed basis, with the medication only taken on nights when symptoms occur. This can range from a few nights per month to nightly, depending on patients' needs. Non-nightly semiflexible dosing is recommended as a prospective action, when a patient anticipates experiencing a bad night. This type of dosing is recommended for a limited number of nights per week. Non-nightly fixed dosing incorporates taking the medication on certain, fixed days of the week. This type of dosing is also restricted to a limited time period. Flexible-timing dosing allows the patient to administer medication once he or she is lying in bed and experiencing difficulties sleeping. Flexible-timing dosing differs from non-nightly flexible dosing in that the patient's flexible timing allows for a patient to initiate therapy at any point in the middle of the night or after awakening and unable to fall asleep again, whereas non-nightly flexible dosing is taken before sleep initiation. All of these strategies are a deviation of past trends of continuous dosing with hypnotics.[21]

Due to the pathophysiology of insomnia, pharmacologic intervention aimed at normalizing the HPA may be beneficial for treating the underlying disturbance in CRF associated with insomnia. Given that HPA axis hyperactivity inhibits sleep and increases awakenings (an effect mediated by increased levels of nocturnal CRF and norepinephrine), and that elevated levels of nocturnal cortisol reported in insomnia are markers of elevated CRF levels, normal sleep patterns may be restored by decreasing nocturnal levels of CRF. Further exploration is warranted into the use of antiglucocorticoid agents for possible treatment of insomnia.

Conclusion

Recognizing the physiologic changes underlying primary insomnia and the resultant morbidity, strategies are evolving that address previous treatment issues. Current management trends reflect a change from considering insomnia a symptom to treating insomnia as a disorder.

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