The Changing Perspective on Chronic Insomnia Management

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A particular challenge in the treatment of insomnia is management of chronic insomnia, which occurs in a substantial portion of the population. A number of factors suggest the importance of identifying this condition as distinct from short-term insomnia in clinical practice and treating these 2 entities differently. Yet, there is no consensus about how to make this distinction or how to manage patients beyond the short term. Clinicians have been without guidance as to how to address the significant challenges associated with treating patients long term with any of the currently available treatments. In recent years, however, new studies have suggested the emergence of a changing perspective on the management of chronic insomnia. These studies have begun to provide an empirical basis for making decisions in the treatment of patients with chronic insomnia. They suggest that clinical practice is evolving toward an improved capacity to treat insomnia, with treatments that can safely lead to sustained efficacy. *(J Clin Psychiatry 2004;65[suppl 8]:20–25)*

The clinical management of patients with insomnia is associated with a number of challenges, one of which is the treatment of the many individuals with chronic insomnia. There is growing evidence that chronic insomnia is highly prevalent and that patients with this condition represent a large percentage of individuals with insomnia. Population surveys indicate that of the 50% of people who report sleep difficulties, 20% to 36% report a duration of difficulties of greater than 1 year.[1–6] Chevalier and colleagues[7] found that the median duration of severe insomnia (defined as sleep difficulties on at least 3 nights per week associated with adverse daytime effects) was 2 to 5.8 years in 5 Northern European countries. In another European study of 2512 general practice patients aged 18 to 65 years,[8] more than 66% of those meeting the *Diagnostic and Statistical Manual of Mental Disorders*, Third Edition, Revised (DSM-III-R) insomnia criteria had a duration of difficulties lasting at least 1 year. Of those patients who reported severe insomnia, 52% still reported moderate to severe insomnia after 2 years. There is some evidence that long-lasting insomnia may be even more prevalent in the elderly.[9] In one study, 57% of general practice patients older than 65 years of age (N = 330) met DSM-III-R criteria for insomnia, and more than 80% of those reported suffering from insomnia for more than 1 year.[9]

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While these data suggest that long-lasting insomnia is highly likely to be encountered in clinical practice, managing such patients has been problematic. In this article, I review the challenges facing the clinical management of chronic insomnia and discuss how new research suggests a changing perspective on the management of this highly prevalent condition.

THE DISTINCTION BETWEEN SHORT-TERM AND CHRONIC INSOMNIA

A number of factors suggest that it is important in clinical practice to identify chronic insomnia as distinct from short-term insomnia and to promote the unique treatment of these 2 entities. First, many key studies of insomnia treatment distinguish between short-term and chronic insomnia. Such studies select a group of patients defined as having either transient or chronic insomnia and target treatments to address the identified condition (see, for example, Hajak et al.,[10] Cluydts et al.,[11] Ware et al.,[12] Scharf et al.,[13] Morin et al.,[14] Pasche et al.,[15] and Friedman et al.[16]).

Second, a distinction is made between acute, subacute, and chronic insomnia for all subtypes of insomnia in one of the most important sleep diagnostic systems, the International Classification of Sleep Disorders (ICSD).[17,18] While the significance of this distinction is not explained, the ICSD states that this distinction may generally be an important basis for differences in the approach to treatment.

Another important factor is the labeling of treatments approved by the U.S. Food and Drug Administration (FDA) for insomnia. In accordance with long-standing treatment guidelines, now considered obsolete by the

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Table 1. ICSD Temporal Definition of Chronic Insomnia by Diagnosis[a]

Psychophysiologic insomnia, sleep-state misperception, environmental insomnia, anxiety disorders associated with insomnia, panic disorder associated with insomnia, insomnia associated with COPD
Acute = 1 mo or less
Subacute = 1 to 6 mo
Chronic = More than 6 mo
Inadequate sleep hygiene, adjustment insomnia, limit-setting insomnia, food allergy insomnia, toxin-induced insomnia
Acute = 1 wk or less
Subacute = 1 wk to 3 mo
Chronic = more than 3 mo
Idiopathic insomnia
Acute = N/A
Subacute = N/A
Chronic = 1 y or longer
Altitude insomnia, sleep-related gastroesophageal reflux
Acute = 1 wk or less
Subacute = 1 wk to 1 mo
Chronic = 1 mo or longer
Sleep onset association disorder
Acute = 3 mo or less
Subacute = 3 to 6 mo
Chronic = more than 6 mo
Hypnotic-dependent insomnia, alcohol-dependent insomnia, insomnia associated with cerebral degenerative disorders
Acute = 3 mo or less
Subacute = 3 mo to 1 y
Chronic = more than 1 y
Stimulant-dependent insomnia
Acute = 3 wk or less
Subacute = 3 wk to 6 mo
Chronic = 6 mo or longer
Psychosis associated with insomnia, mood disorder associated with insomnia
Acute = 4 wk or less
Subacute = 4 wk to 2 y
Chronic = more than 2 y
Fatal familial insomnia
Acute = 1 mo or less
Subacute = 1 mo to 1 y
Chronic = N/A

[a]Based on Diagnostic Classification Steering Committee.[17,18]
Abbreviations: COPD = chronic obstructive pulmonary disease, ICSD = International Classification of Sleep Disorders.

National Institutes of Health, all of the agents currently approved for the pharmacologic treatment of insomnia are indicated only for short-term use.[19,20] While the guidelines and FDA labeling address duration of treatment rather than duration of disease, they promote a distinction between short-term and chronic insomnia, implying that short-term and chronic insomnia should be treated differently.

The Problem of Defining Chronic Insomnia

While these factors promote the clinical identification of patients with chronic insomnia, no consensus currently exists on how this condition should be identified. There are substantial differences in how this issue is addressed in the major sleep diagnostic systems, and widely varying definitions are found in insomnia research studies.

The 2 most important sleep diagnostic systems are the ICSD[17,18] and the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (DSM-IV).[21] In the ICSD, the duration that defines chronic insomnia differs among insomnia subtypes (Table 1). The level of complexity of this system impedes its use in most clinical settings.

The DSM-IV approaches insomnia in an entirely different way.[21] This system does not acknowledge insomnia of less than 4 weeks' duration, and does not otherwise differentiate insomnia with regard to duration, although it mentions that in clinical practice a chronic phase is frequently seen that lasts for many years. In terms of insomnia subtypes, primary insomnia and insomnia due to another mental disorder are defined as requiring at least 1 month of sleep difficulties.[21] The only other insomnia subtype, where sleep difficulties are due to a general medical condition, has no specified duration.[21] Such global definitions are easy to implement clinically but do not provide any guidance regarding the definition of chronic insomnia.

The lack of a consensus about whether or how to distinguish chronic from short-term insomnia evident in the diagnostic systems is also apparent in the insomnia research literature. In these studies, the inclusion criteria aimed at the identification and treatment of patients with chronic insomnia differ widely. The most common requirements for inclusion are a duration of difficulties of 1 month,[10,11] 3 months,[12,13] and 6 months.[14–16]

Unfortunately, in addition to the absence of a consensus in the diagnostic systems and research literature, there are no research data that could serve as a basis for a definition of chronic insomnia for practitioners. In fact, it remains unclear from existing research whether there is indeed a natural division between short-term and chronic insomnia and whether differentiation of insomnia with respect to duration is a clinically meaningful construct.

THE CHALLENGE OF CHRONIC INSOMNIA TREATMENT

The current state of affairs leaves clinicians without guidance as to how or whether to distinguish between short-term and chronic insomnia and how to manage insomnia patients when their difficulties extend beyond the short-term period. When clinicians decide to pursue longer-term insomnia treatment, they have to choose from a set of options, each of which is associated with significant challenges. These options include long-term treatment with hypnotic medications; off-label treatment with sedating antidepressant, antipsychotic, or antihistamine medications; nonpharmacologic therapies; and no treatment at all.

Long-Term Insomnia Treatment With Hypnotic Medications

As mentioned earlier, hypnotics are the only agents currently approved by the FDA for the treatment of insomnia.

This includes medications from the benzodiazepine class, as well as the nonbenzodiazepines zolpidem and zaleplon. Many practitioners may be concerned about prescribing these medications long term because of the clinical guidelines that discourage treatment beyond several weeks. An additional deterrent is the prevalent concern about dependence and abuse with these agents, which is heightened with respect to longer-term treatment.[19] The hesitation to use such medications in longer-term treatment in clinical practice has been invoked to explain data demonstrating the declining use of benzodiazepines and the concomitant rise in antidepressant use for the treatment of insomnia.[22] Use of antidepressants, which are perceived as safer for long-term insomnia treatment, increased by 146% from 1987 to 1996, while hypnotic medication use declined by 53.7% during the same period.[22]

Concerns about long-term treatment are likely to cause a decrease in even short-term use of these medications because there are currently no data that allow clinicians to predict which insomnia patients will require longer-term treatment. In this regard, data are needed to indicate predictors of success in periodic attempts to discontinue hypnotic medications, beginning with the first month of treatment. Without such data, the prevalent concerns about dependence are likely to discourage use of hypnotic medications, specifically a perception of a high likelihood of nontherapeutic use, and a risk of rebound insomnia and withdrawal symptoms foiling attempts to discontinue the medication[23] and thereby leading to longer-term use.[8,24–27]

It is notable that all of these concerns about long-term hypnotic treatment exist even though there is a striking absence of research regarding treatment beyond the recommended time period. In fact, there have been no large-scale placebo-controlled studies of the treatment of insomnia with hypnotic medications for longer than 5 weeks' duration.[27] Thus, while the widespread concerns about long-term hypnotic treatment have not been rooted in empirical evidence, there has been no experimental basis for clinicians to be confident of the efficacy or safety of these medications in long-term treatment.

The Treatment of Chronic Insomnia With Antidepressants, Antipsychotics, and Antihistamines

While there are few data on the long-term treatment of insomnia with hypnotic medications, there is even less empirical support for the treatment of chronic insomnia with antidepressants, antipsychotics, and antihistamines. In fact, there is a near total absence of studies of even the short-term treatment of insomnia with these medications, including some of the most prescribed antidepressant medications, such as trazodone.[22,28] In addition, these medications are associated with side effects that may be problematic, and there is some recent evidence that antihistamines appear to lose efficacy after only a few days of treatment.[29]

The Treatment of Insomnia With Nonpharmacologic Therapy

Nonpharmacologic therapies (e.g., cognitive-behavioral therapy) have long been available for the treatment of insomnia, and a number of studies suggest their efficacy.[30] However, pharmacologic therapy has been used clinically much more frequently, especially in the primary care setting.[30,31] Two reasons for the less frequent use of the nonpharmacologic therapies in primary care may be that they are time intensive and require significant training for effective implementation.[32]

Choosing Not to Treat Chronic Insomnia

Faced with these challenges, it would be understandable for some clinicians to elect not to institute any therapy for long-lasting insomnia. One important factor promoting this decision is the lack of studies demonstrating that any of the available treatments have sustained efficacy in the long-term treatment of insomnia. This is because, without evidence of significant benefit, there is nothing to offset the above challenges when making a risk-benefit decision about whether to institute treatment.[27] Similarly, evidence that untreated chronic insomnia leads to significant adverse consequences has been limited. The absence of evidence of significant impairment would also tend to promote a decision not to treat insomnia given the perceived risks and challenges.

THE CHANGING LANDSCAPE

All of these considerations suggest that clinicians face a significant challenge in the treatment of chronic insomnia. A number of recent studies indicate a changing perspective on the treatment of this condition, prompted by growing evidence of the consequences of untreated insomnia, controlled studies of nonpharmacologic therapies and the exploration of less time-intensive therapies, an improved understanding of the risks of dependence and nontherapeutic use associated with hypnotic agents, and the recent appearance of studies of the longer-term pharmacologic treatment of insomnia.

Adverse Effects of Untreated Insomnia

A growing body of evidence suggests that untreated chronic insomnia is associated with a host of adverse effects.[33–40] Zammit[33] found impaired quality of life, cognitive function, and occupational functioning in 261 subjects with insomnia compared with normal controls (N = 101). Cricco et al[38] determined that chronic insomnia was related to impaired cognitive functioning among men in their cohort of more than 6000 elderly subjects, aged 65 years and older. One recent study found that chronic sleep difficulties predicted mortality related to coronary artery disease in men.[37] Other studies have demonstrated that chronic insomnia predicts the onset of new psychiatric

disorders such as depression, posttraumatic stress disorder, and a number of other diseases.[36,39] This predictive association between depression and chronic insomnia is the most well-established link between a psychiatric disorder and insomnia.[34,39–41]

These adverse consequences of untreated chronic insomnia, along with recent evidence that treatment with hypnotic medications can lead to a significant improvement in daytime function ratings in this population,[42] provide empirical support for a change in the risk-benefit ratio in favor of the treatment of insomnia. These data speak to the adverse consequences of not treating insomnia and provide preliminary evidence that treatment may decrease these risks by demonstrating that the benefits of treatment extend beyond the improvement of sleep into a number of important areas of functioning. Further studies will be needed to determine the extent to which the many adverse consequences of chronic insomnia are addressed by treatment of this condition.

Developments in Nonpharmacologic Therapy

Recent research studies have the potential to improve the capacity of nonpharmacologic therapies to make a significant contribution to the clinical treatment of insomnia. The last several years have contributed further controlled studies suggesting the efficacy of nonpharmacologic therapies for the treatment of insomnia. However, lack of access to treatment rather than efficacy appears to be the major factor limiting the impact of these treatments for insomnia.[32,43–45] In this regard, some groups have been working to develop briefer forms of nonpharmacologic therapy that are tailored for use in the primary care setting,[32] where the preponderance of insomnia treatment occurs. Further work on these briefer treatments may allow an increased number of patients with insomnia to have access to nonpharmacologic therapies as a treatment option.

Developments in Understanding the Risks of Dependence and Nontherapeutic Use of Hypnotics

Concerns about dependence and the nontherapeutic use of benzodiazepines have been an important factor in limiting the long-term treatment of insomnia with hypnotic medications.[19,23] However, a series of studies has suggested that the risks of dependence and recreational use, particularly with the nonbenzodiazepine agents, are relatively low in insomnia patients. In this regard, there is evidence that insomnia patients use hypnotic medications for therapeutic effect and do not engage in recreational use or drug-seeking behavior.[46–49] Dose escalation appears to occur only when treatment is ineffective at alleviating insomnia[46] and when the patient has a history of substance abuse or anxiety.[50] In addition, there is evidence that the risk of dependence and abuse associated with the nonbenzodiazepine hypnotic agents may be lower than that associated with benzodiazepine hypnotics.[50–52] Preliminary data on nontherapeutic use in drug abusers are also consistent with lower risks with nonbenzodiazepine medications.[53] Thus, in insomnia patients without significant anxiety or a history of substance abuse, the risks of nontherapeutic use and dependence or abuse with nonbenzodiazepine hypnotics appear to be relatively low. Like other, more recently understood information regarding insomnia and its management, these new data may herald a change in thinking so that hypnotic treatment is perceived to have a more favorable risk-benefit ratio.

Studies of Longer-Term Medication Treatment of Insomnia

Another important development has been the recent completion of studies of the longer-term medication treatment of insomnia. In particular, 2 studies provide compelling evidence of the safety and efficacy of the longer-term treatment of insomnia with nonbenzodiazepine hypnotic medications.[54,55] One study examined nightly open-label treatment with zaleplon for 1 year in 476 primary insomnia elderly patients and demonstrated favorable safety with nightly use over a year-long period.[54] The other study was a 6-month randomized, double-blind, placebo-controlled trial of eszopiclone in 788 primary insomnia sufferers, followed by a 6-month open-label treatment phase.[55] The placebo-controlled phase of the eszopiclone study provided robust evidence of sustained efficacy in self ratings of sleep onset, sleep maintenance, and daytime functioning, with no evidence of tolerance over 6 months. Safety data indicated favorable safety over the 6-month double-blind phase and then over the additional 6-month open-label phase. The fact that no significant dependence-related phenomena were found in either study is consistent with the data described above, suggesting a low risk of dependence and dose escalation with nonbenzodiazepine medications. In addition, these studies suggest that there is no unfavorable transition in the risk-benefit ratio for treatment occurring around 3 to 4 weeks, which is implicit in the long-standing clinical guidelines.[19] In summary, these studies demonstrate that hypnotic medications can be safe and lead to sustained efficacy in the long-term treatment of insomnia. These findings, along with the data presented earlier, suggest the emergence of an empirical foundation for an improved capacity to treat chronic insomnia.

CONCLUSIONS

It is clear that long-lasting insomnia is highly prevalent and associated with adverse sequelae. Yet, the treatment of this condition faces a number of significant challenges. Several factors provide an impetus to view patients with chronic insomnia differently from the rest of insomnia patients; however, there has been no consensus as to how to identify these patients or how to manage them. Further, the

available treatment options have all been associated with significant limitations, primarily based on an absence of data on the efficacy and safety of long-term treatment. However, recent studies have improved our understanding of insomnia and its treatment and suggest a changing perspective on the management of chronic insomnia. This includes a greater appreciation of the adverse effects of untreated insomnia, developments in nonpharmacologic therapies, better understanding of the risks of dependence/abuse and nontherapeutic use of hypnotic agents, and large-scale studies suggesting the safety and efficacy of longer-term nightly treatment with nonbenzodiazepine hypnotic medications. These studies have begun to provide an empirical basis for making decisions in the treatment of patients with chronic insomnia. These studies, which suggest that treatments exist that can safely lead to sustained efficacy in the treatment of insomnia, provide a gateway to further research needed to improve the capacity to treat this condition in clinical practice.

Drug names: trazodone (Desyrel), zaleplon (Sonata), zolpidem (Ambien).

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