

Insomnia in Women

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Insomnia is a highly prevalent disorder that can lead to substantial impairments in quality of life and functional capacity. This condition occurs significantly more frequently in women than men. An important contributing factor is that insomnia can occur in association with hormonal changes that are unique to women, such as those of menopause or the late-luteal phase of the menstrual cycle. Another consideration is that women are more likely to suffer from major depression and anxiety disorders, which are also associated with insomnia. The reasons are unclear as are the reasons why women are at increased risk of primary insomnia. These conditions are frequently encountered in clinical practice and present a challenge to the practitioner because there is a striking lack of research data to serve as a guide. For example, there are no published studies to indicate how to safely and effectively manage insomnia that often occurs late in pregnancy. This article reviews the available literature related to these conditions with a focus on the epidemiologic data and diagnosis and treatment of insomnia and highlights the need for further research. Clinical Cornerstone Vol. 5, No. 3. Copyright © 2003 Excerpta Medica, Inc.

Insomnia is a highly prevalent disorder characterized by difficulty in falling or staying asleep or nonrestorative sleep occurring in the setting of significant distress or impairment in function (1). It is estimated that 10% to 27% of the population suffer from this condition (2,3); among primary care patients the prevalence appears to be even greater (4). Increasing evidence indicates this condition leads to fundamental impairments in quality of life and functional capacity and represents a substantial economic burden (5–7). As these data have been accruing, it has also become increasingly apparent that insomnia is much more common in women than in men (Table I) (3).

The reasons why women are more likely to suffer from insomnia are not completely understood. Evidence suggests that insomnia can occur in association with hormonal changes that are unique to women, such as those accompanying menopause or the late-luteal phase of the menstrual cycle (1,8). Although the relationship between hor-

mone levels and sleep is complex, there appears to be an association between a decrease in circulating estrogen and progesterone and an increased propensity to insomnia (9–11). Progesterone has been found to have a sedative effect when administered intravenously, though it is unclear if this explains the propensity to insomnia when progesterone levels fall, as has been proposed (12,13).

KEY POINT

Evidence suggests that insomnia can occur in association with hormonal changes that are unique to women, such as those accompanying menopause or the late-luteal phase of the menstrual cycle.

Another factor contributing to the relatively high rate of insomnia among women is that they

TABLE I. MAJOR CAUSES OF INSOMNIA IN WOMEN AND THEIR PREVALENCE

<i>Cause of Insomnia</i>	<i>Prevalence</i>
Premenstrual insomnia	Unknown, though many of the estimated 3% to 5% of women with premenstrual dysphoric disorder have insomnia (1)
Perimenopausal and postmenopausal insomnia	30% to 60% of women report insomnia in this setting. How often there is a link with menopausal hormone changes is unknown (11,21).
Insomnia in pregnancy	Unknown, though believed to be highly prevalent in the 3rd trimester
Insomnia in the setting of psychiatric disorders	Probably highly prevalent. The most common disorder is major depression where women have a lifetime risk of 10% to 25% (1).
Primary insomnia	~ 1% (8)

are more likely to suffer from psychiatric disorders, such as major depression and anxiety, which are highly correlated with insomnia (1,8). The fact that an increase in anxiety and depressive symptoms is reported by many women in the late-luteal phase as well as in the perimenopausal and postmenopausal periods suggests that hormonal changes may also play a role in the increased risk of psychiatric disorders in women (1,11). There are no data that meaningfully address this speculation.

It is also not known why primary insomnia is more prevalent in women (8). Primary insomnia is a condition where insomnia occurs without the presence of an underlying causative disease, medication, or substance. Although study of the pathophysiology of this condition has advanced, why it affects women more has not been identified.

In each of these conditions, an overrepresentation of women is quite evident. However, it is also apparent that the pathophysiologic mechanisms remain unknown, which reflects the striking lack of research related to insomnia in women (11). The paucity of research leaves practitioners without much guidance as to how to manage their female patients with insomnia. For example, there are no published studies to indicate how to safely and effectively manage the insomnia that frequently occurs late in pregnancy (14).

In this article, the research data available in each of these conditions are reviewed. That there is no consensus as to whether some of these difficulties should be considered disorders speaks to the inadequacy of the available data. While the focus

is on epidemiologic, diagnostic, and treatment issues, the overarching conclusion of this review is that more research studies are needed.

KEY POINT

The decision to treat women with sleep problems should be based on an assessment of the level of distress or impairment in function.

PREMENSTRUAL (LATE-LUTEAL PHASE) INSOMNIA

Difficulties with both insomnia and excessive sleepiness are sometimes reported by women in association with the premenstrual (late-luteal) phase of their menstrual cycle (1,15). Menstrual cycle-related sleep difficulties are often considered in the context of premenstrual mood or anxiety difficulties. There is some uncertainty about whether these difficulties constitute a formal disorder. A syndrome termed *premenstrual dysphoric disorder* was proposed for inclusion in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)* but was not included. Instead, it was included in the category of entities provided “for further study” because it was believed there was insufficient information to warrant inclusion as an official *DSM-IV* disorder (1). The published proposed diagnostic criteria require that 5 of a pro-

TABLE II. DSM-IV CRITERIA FOR PREMENSTRUAL DYSPHORIC DISORDER

- A. In most menstrual cycles during the past year, 5 (or more) of the following symptoms were present for most of the time during the last week of the luteal phase, began to remit within a few days after the onset of the follicular phase, and were absent in the week postmenses, with at least 1 of the symptoms being either (1), (2), (3) or (4):
- (1) markedly depressed mood, feelings of hopelessness, or self-deprecating thoughts
 - (2) marked anxiety, tension, feelings of being “keyed up,” or “on edge”
 - (3) marked affective lability (eg, feeling suddenly sad or tearful or increased sensitivity to rejection)
 - (4) persistent and marked anger or irritability or increased interpersonal conflicts
 - (5) decreased interest in usual activities (eg, work, school, friends, hobbies)
 - (6) subjective sense of difficulty concentrating
 - (7) lethargy, easy fatigability, or marked lack of energy
 - (8) marked change in appetite, overeating, or specific food cravings
 - (9) hypersomnia or insomnia
 - (10) a subjective sense of being overwhelmed or being out of control
 - (11) other physical symptoms, such as breast tenderness or swelling, headaches, joint or muscle pain, a sensation of “bloating,” weight gain
- Note: In menstruating females, the luteal phase corresponds to the period between ovulation and the onset of menses, and follicular phase begins with menses. In nonmenstruating females (eg, those who have had a hysterectomy), the timing of luteal and follicular phases may require measurement of circulating reproductive hormones.
- B. The disturbance markedly interferes with work or school or with usual social activities and relationships with others (eg, avoidance of social activities, decreased productivity, and efficiency at work or school).
- C. The disturbance is not merely an exacerbation of the symptoms of another disorder, such as major depressive disorder, panic disorder, dysthymic disorder, or a personality disorder (although it may be superimposed on any of these disorders).
- D. Criteria A, B, and C must be confirmed by prospective daily ratings during at least 2 consecutive symptomatic cycles. (The diagnosis may be made provisionally prior to this confirmation.)

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vided list of 11 sets of symptoms be present in the late-luteal phase of the majority of menstrual cycles in the previous year (**Table II**). These symptoms must begin to remit within a few days after onset of the follicular phase and disappear in the week after the menstrual period. Sleep difficulties are reflected in the premenstrual dysphoric disorder definition only in that 1 of the 11 symptom sets listed in the proposed diagnostic criteria is “hypersomnia or insomnia.”

One implication of this proposed definition that is particularly relevant is that a woman having recurrent premenstrual insomnia without any other difficulties would not meet the criteria for the proposed disorder. The extent to which this type of

difficulty is reported cannot be determined from available data. One study of 32 healthy women suggests that premenstrual insomnia symptoms tend to occur in the absence of other symptoms, whereas women with an elevated incidence of other types of premenstrual symptoms (such as mood and anxiety difficulties) are more likely to report daytime sleepiness than insomnia (15). Further studies are needed to better delineate the symptoms that recur premenstrually and whether there are natural clusters among these symptoms.

The manner in which premenstrual insomnia difficulties are addressed in the *International Classification of Sleep Disorders (ICSD)* diagnostic system reflects a similar degree of uncertainty as is

evident in the *DSM-IV* (8). Premenstrual sleep difficulties are not included among the established sleep disorders but are included as a proposed sleep disorder entitled “Menstrual-Associated Sleep Disorder.” This condition is defined as a complaint of insomnia or episodes of excessive sleepiness that are temporally related to the menstrual cycle and are present for at least 3 months (8).

Polysomnographic (PSG) evidence of reduced sleep efficiency, reduced total sleep time, and frequent awakenings as well as the absence of an underlying medical, mental, or sleep disorder are also diagnostic criteria. The origin of the proposed PSG requirement is unclear. While PSG changes have been reported across the menstrual cycle in a number of studies, they are not found consistently (16,17). This part of the proposed definition presents the practitioner with a number of challenges. The proposed diagnostic criteria could not be implemented in clinical practice without referring patients for a PSG, which is currently not recommended in the evaluation of insomnia unless there is a suggestion of sleep apnea or periodic limb movements (18). Another problem with the requirement is that even if a PSG were carried out, it would be difficult to implement the proposed criteria because there is no consensus as to what constitutes a “reduced sleep efficiency, reduced total sleep time, or elevated number of awakenings.” These difficulties again speak to the need for more research in this area.

In lieu of research data, it is necessary to take a pragmatic approach to clinical management. It seems reasonable to manage premenstrual complaints of disturbed sleep similarly to sleep difficulties in other contexts. If problems with sleep initiation, maintenance, or quality occur in frequent association with the late-luteal phase of the menstrual cycle, further inquiry should be triggered. The decision to treat should be based on an assessment of the level of distress or impairment in function (1).

When a decision has been made to treat this type of insomnia, several options can be considered. The most commonly employed treatment for clinically significant premenstrual difficulties is selective serotonin reuptake inhibitors (SSRIs), which have been demonstrated in a number of stud-

ies to be efficacious in the treatment of premenstrual dysphoric disorder (19). Whether SSRIs targeted to the syndrome of premenstrual dysphoric disorder would be helpful in those patients complaining of insomnia is not known. It is notable that SSRIs have been approved for use in premenstrual dysphoric disorder for both continuous and intermittent dosing schedules despite the fact that this condition does not have the status of a disorder in the psychiatric diagnostic system (1,19). Another treatment option is the administration of sedative/hypnotic medication.* In instances where insomnia is prominent or the only symptom, there are reasons why sedative/hypnotic medication may be preferable to SSRIs, which are less likely to be effective as treatment for insomnia in general and may actually cause insomnia as a side effect (20). Also, the sedative effect of SSRIs may, like the antidepressant effect, become evident only after several weeks of treatment. As a result, the sedative/hypnotics, which are well established to improve insomnia after the first dosage, might be a better choice for use in a several-day-monthly treatment regimen.

KEY POINT

Further studies are needed to better delineate the symptoms and disorders that accompany perimenopausal and postmenopausal insomnia.

PERIMENOPAUSAL AND POSTMENOPAUSAL INSOMNIA

Like premenstrual sleep difficulties, there are limited data on insomnia in women that occurs in conjunction with perimenopausal and postmenopausal changes. Thus, this condition is controversial and

* Author’s Note: While I am aware of no studies of this approach, I have had success in my clinical practice with a short course of sedative/hypnotic medication during the affected period in several cases of recurrent, isolated premenstrual insomnia. A short course of sedating antidepressant medication could be explored as well.

is not represented among the disorders included in the major sleep or psychiatric diagnostic systems (1,8). In the *ICSD* these difficulties are included under “Menstrual-Associated Sleep Disorder,” included among the proposed sleep disorders. The criteria and the problems associated with the PSG component have been discussed. Here, the sleep difficulties are in temporal association with the menopause rather than recurrently in the premenstrual period (8). Understanding of this condition is clouded by the concomitant occurrence of other symptoms and disorders, such as anxiety, depression, sleep apnea, and periodic waking and sleep episodes, which are frequently seen in women in the perimenopausal and postmenopausal periods (11). Controversy exists about how best to define and understand, in particular, the psychiatric symptoms involved in this setting. However, a consistent body of research data suggests that sleep maintenance difficulties develop in peri- and postmenopausal women in association with nocturnal vasomotor events (eg, hot flashes at night) (11). The prevalence of these difficulties is unknown, but preliminary evidence shows that the number of affected women is quite large. It has been reported that 30% to 60% of peri- and postmenopausal women complain of insomnia (11,21).

Evaluation of women with complaints of sleep difficulties occurring in this setting should include assessment for sleep apnea, periodic movements in sleep, restless legs syndrome (RLS), major depression, anxiety disorders, insomnia that predates hormonal changes, and any other underlying difficulties that may be causative (11). If the evaluation suggests apnea or periodic movements in sleep, or if the origin of the sleep dysfunction is unclear, referral to a sleep center should be considered. If a condition such as anxiety or depression is identified, that underlying condition should be treated. The diagnosis of peri- or postmenopausal insomnia appears to be most warranted when there is evidence that the onset of the insomnia symptoms coincided with a change in the regularity of menstrual periods and/or vasomotor symptoms and that nocturnal awakenings are occurring in conjunction with night sweats (11).

One challenging aspect of the diagnostic

process is that insomnia may sometimes be the first or only presenting symptom of peri- or postmenopausal difficulties (11). Furthermore, women suffering from insomnia often do not mention this to their health care practitioner. In light of the high incidence of insomnia in peri- and postmenopausal women, patients who report vasomotor events or changes in their menstrual cycles should be asked about the quality of their sleep. While a physiologic screening test would be particularly useful in this circumstance, there are no current diagnostic procedures that can be used clinically to definitively identify whether insomnia symptoms are linked to peri- and postmenopausal hormonal changes (11).

As these sleep difficulties are believed to be due to diminished circulating levels of estrogen and progesterone, it is natural to consider hormone replacement therapy (HRT) for the treatment of this condition. However, this approach has significant limitations. Some women prefer not to take HRT because of health risks or medical contraindications, and it is not universally effective (11). Also, vasomotor symptoms appear to improve more consistently than sleep difficulties. Therefore, the practitioner should consider whether other factors or underlying causes may be contributing to the insomnia.

Another consideration is whether behavioral factors may be playing a role. One such scenario is the development of a classically conditioned insomnia (11), which can occur with any cause of transient sleep disruption. It is characterized by insomnia continuing after the causative problem has been eliminated and is believed to be triggered by repeated struggles with sleep, particularly in the same environment. This process links the frustration, anger, and anxiety associated with sleep difficulty to the process of sleep or the sleep environment in such a way that engaging in the sleep process or entering the bedroom can spontaneously elicit the feelings and thereby perpetuate the sleep difficulty. Cognitive behavioral therapy for insomnia, which has been demonstrated to be effective in placebo-controlled trials, is the treatment of choice in this circumstance (22). This therapy addresses the conditioned insomnia by minimizing the time affected women spend in bed awake, addressing their coun-

terproductive beliefs about sleep and emotional reaction to sleep difficulties, and restricting their sleep time to increase the likelihood that they will be tired when they attempt to sleep. However, no data exist on the effectiveness of this treatment in the setting of peri- or postmenopausal insomnia.

In some instances it may be useful to consider pharmacotherapy for peri- and postmenopausal insomnia. Few studies of medication management of this condition have been conducted. One open-label trial of 75-mg trazodone (N = 25) suggested that this medication might have some efficacy (23). Recently, a randomized, double-blind, placebo-controlled trial of 10-mg zolpidem was undertaken. Preliminary analysis of this trial shows efficacy and safety in the treatment of peri- and postmenopausal insomnia (unpublished data). It is obvious that more studies are needed. The challenges faced in choosing an agent for the pharmacologic treatment of peri- and postmenopausal insomnia are the same as for the clinical management of insomnia in other settings (24). The existing literature on medication management of insomnia is particularly limited with regard to long-term treatment and the management of sleep maintenance difficulties of peri- and postmenopausal patients.

INSOMNIA IN PREGNANCY

Insomnia in pregnancy tends to occur in the third trimester, which appears to be due to a number of factors that are likely in the later stages of pregnancy, including discomfort, back pain, urinary frequency, fetal activity, periodic movements in sleep, and RLS (14). Like premenstrual, perimenopausal, and postmenopausal sleep difficulties, insomnia in pregnancy is represented as a proposed sleep disorder in the diagnostic schema (8). The proposed criteria for “Pregnancy-Associated Sleep Disorder” specify that insomnia begins and is present during pregnancy along with PSG evidence of frequent arousals, reduced sleep efficiency, and the absence of other underlying causative disorders. As with the 2 preceding disorders discussed, there is limited research on this common condition. No data exist to guide the practitioner as to when to intervene or how to institute treatment. It has been suggested that behavioral sleep interventions are often effective

in this setting and should be the first-line therapy (14). These interventions include relaxation techniques, optimizing sleep hygiene (eliminating behaviors that tend to promote insomnia such as irregular sleep/wake schedule, napping, caffeine use, etc.), and “stimulus-control therapy” where the goal is to minimize the time spent in bed awake, which is meant to prevent linking the frustration/anger/arousal that may occur with repeated difficulties in falling or staying asleep in the bedroom environment via classical conditioning. In cases where these nonpharmacologic therapies are not effective, the use of zolpidem or diphenhydramine has been suggested, though again no data exist on their use (14). The guiding principle for all decisions in this setting is to maximize the safety of the fetus and the mother.

INSOMNIA WITH DEPRESSION AND ANXIETY DISORDERS

Women are twice as likely as men to suffer from major depression and comprise 66% of individuals with anxiety disorders (1,8). Both of these conditions are frequently associated with insomnia. It is estimated that insomnia occurs in ~75% of individuals with major depression (8); therefore, careful screening of women for anxiety and depressive symptoms is necessary in the primary care setting. Further, when such symptoms are discerned, it is important to assess for the presence of insomnia. Treatment of women with depressive or anxiety disorders begins with instituting the standard pharmacologic therapies for these conditions. For major depression, this would be the administration of antidepressant medications. For anxiety disorders, the most appropriate treatment will depend on the particular disorder present; common pharmacologic therapies include antidepressants, benzodiazepines, and buspirone. Unfortunately, there are insufficient studies to provide guidelines as to when to institute treatment specifically for insomnia that occurs regularly in this setting. An adequate discussion of the management of insomnia in mood and anxiety disorders is beyond the scope of this review. However, a few comments on the relationship of insomnia and depression may be useful.

A number of factors suggest the importance

of effectively and rapidly treating insomnia in patients with depression. Growing evidence points to insomnia as a risk factor for depression (25,26). Further, there is some preliminary evidence that residual insomnia following successful treatment of depression may increase the risk of relapse. Preliminary data also suggest that instituting treatment for insomnia in conjunction with commencing antidepressant therapy may speed the alleviation of depression (27). There is a growing appreciation of the importance of effectively treating insomnia associated with depression, but further studies are needed to determine how to optimally implement treatment.

The optimal way to manage insomnia in the setting of depression remains unknown. Options include a sedating antidepressant, a nonsedating antidepressant along with a sedating antidepressant, or a nonsedating antidepressant and a sedative/hypnotic agent (28). A few preliminary studies suggest that trazodone and zolpidem may be effectively used when administered in conjunction with a nonsedating antidepressant agent for this purpose (20,29,30). No data exist comparing these 2 treatment options. One consideration is that the efficacy and safety of zolpidem in the treatment of insomnia are much better established than for trazodone, which has been the subject of little insomnia research. In terms of side effects when combined with an SSRI, while no significant problems were reported for either medication in the few available studies, the combination of trazodone and an SSRI brings with it an increased risk of precipitating serotonin syndrome (20,29,30). Also, zolpidem and trazodone differ in their half-lives such that the longer-acting trazodone is more likely to lead to next-day residual impairment, whereas zolpidem is more likely to not last long enough to address the early morning sleep problems in some patients.

PRIMARY INSOMNIA

Although primary insomnia is more common in women than in men, this condition occurs relatively infrequently in the population, having a prevalence of 1% to 2% (8). However, the increased prevalence of primary insomnia in women is not only interesting but unexplained. This diagnosis is made

when insomnia criteria are met in the absence of an underlying causative condition such as depression, anxiety, medication effect, or substance abuse. (1,8).

Pharmacologic management and cognitive behavioral therapy are the principal treatments of primary insomnia (22,24). Again, no data are available to help determine when to institute pharmacologic versus nonpharmacologic treatment and whether treatment should be tailored to gender.

SUMMARY

Insomnia is a common problem in women. Women preferentially experience insomnia, in the premenstrual period, peri- and postmenopause, the late stages of pregnancy, the setting of anxiety and depression, and in primary insomnia. Little is known about the mechanisms that lead to insomnia in these settings. Because so many women experience sleep difficulties in these settings and because knowledge related to optimal treatment is extremely limited, they represent a substantial clinical challenge. Where insomnia is due to menstrual cycle-related hormonal changes or pregnancy, the reasons for the preferential gender representation are obvious. In the other instances, the reasons for the greater odds of sleep disorders in women are uncertain. Also, it is not known to what extent female overrepresentation reflects the greater likelihood that women report or seek help for their sleep-related problems. The clearest and most prominent conclusion that can be drawn from this review is that more research into these issues is crucial for proper diagnosis and treatment.

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Dialogue Box

EDITORIAL BOARD

Since insomnia is so common, to what do you attribute the dearth of studies pertaining to its pathogenesis and treatment?

KRYSTAL

A number of factors are likely involved. First of all, our culture has tended to downplay insomnia as a problem, viewing it almost as a normal part of life. Certainly insomnia has not been viewed in the same light as coronary heart disease or cancer. As a result, there has been less interest to study it. This probably will change, however, with the growing appreciation of insomnia's association with depression, impaired job performance, absenteeism, and health care utilization. Secondly, a stigma surrounds the treatment of insomnia as a result of past problems with hypnotic agents such as the barbiturates and nonbarbiturate agents such as methaqualone.* As a result, some researchers were so concerned about medication use and abuse that they were reluctant to do a study for fear they might "hook" study subjects on these drugs.

EDITORIAL BOARD

Insomnia is a common component of depression. What are your thoughts regarding the use of sedating antidepressants as first-line therapy?

KRYSTAL

This may be a useful approach for some patients, but for others the side effects can be prohibitive. The alternative is to use a less sedating antidepressant and combine it with a hypnotic agent. This approach allows greater flexibility. If over time there is no longer a need for a sedative effect due

*Not FDA approved.

to a successful antidepressant response, it may be possible to stop the hypnotic without losing prophylaxis against depression relapse. With the single-agent approach, the additional side effects that may be seen with more sedating antidepressants cannot be eliminated without losing the antidepressant effect.

EDITORIAL BOARD

The SSRIs are the most commonly prescribed antidepressants in the United States but not infrequently cause insomnia as a side effect. What do you think of the practice of adding a small dose of a sedating antidepressant, such as trazodone or doxepin, to manage this side effect?

KRYSTAL

There is evidence that many practitioners prefer antidepressant medications over hypnotic agents because of a perception they are safer. When I ask practitioners what the basis of this viewpoint is, they usually indicate greater abuse potential of hypnotics or simply don't know. It turns out that extremely little research has been carried out on the safety and efficacy of sedating antidepressants in the treatment of insomnia. In contrast, there are a large number of studies demonstrating the efficacy and safety of hypnotic medications. There are, however, limited data on the combination of hypnotic medication and SSRIs in the treatment of insomnia associated with depression.

Another consideration is that, in my view, the risk of taking an overdose of the prescribed antidepressant in an attempt to commit suicide is a much more real risk than abuse potential in this setting. In this regard, it is very hard to understand how practitioners could feel that a drug like doxepin is somehow safer than zolpidem. The newer benzodiazepines as a whole are among the

Dialogue Box

safest medications when taken in overdose, whereas an overdose with a tricyclic antidepressant, such as doxepin, is much more likely to be lethal.

EDITORIAL BOARD

Using a short-acting BZRA agent to combat insomnia in a depressed patient taking an SSRI might very well translate into a 9- to 12-month course of treatment. Are there any problems stopping the hypnotic agent once the SSRI is discontinued?

KRYSTAL

Data with regard to stopping hypnotic medications after 9 to 12 months of nightly treatment are somewhat sparse but for the most part reassuring. At the Association of Professional Sleep Society meetings this year, there were 2 posters presented that reported the effect of stopping hypnotic medications “cold turkey” after nightly use over an entire year. One of these studies involved the medication eszopiclone and the other involved zaleplon. Neither of the 2 studies reported significant problems, such as seizures, with sudden cessation of use.

Another concern that is often raised is a greater possibility of abuse when hypnotic medications are taken for longer periods of time. The available data do not support this. Furthermore, if you look at the data available on the potential for abuse of these medications, such as that coming from Tim Roehrs at Henry Ford Hospital, it turns out that dose escalation with the BZRA agents seems to occur only in patients with insom-

nia in whom the medications don't seem to work and in those patients in whom the agent loses its effect over time. In other words, their use appears solely therapeutic. The only exception appears to be individuals with a substance abuse history.

EDITORIAL BOARD

Insomnia is a common complaint voiced by perimenopausal and postmenopausal women. Putting aside the issues raised by the findings of the Women's Health Initiative Study and apart from its effectiveness in treating hot flashes interfering with sleep, does estrogen replacement therapy offer any benefit on sleep?

KRYSTAL

Although data are limited, my view is that it is likely that hormone replacement therapy can improve sleep over and above its favorable impact on vasomotor complaints. What we know about menstrual symptoms suggests that fluctuations in hormones can have a sleep-disruptive effect in some women, which may relate to the broader question of why is it that women have more insomnia and depression than men? In this regard, there is some interesting ongoing neuropharmacologic research that will hopefully help us better understand this relationship. However, in light of recent reports, it is important that the decision as to whether to institute hormone replacement therapy take into account the risks of this form of therapy.

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