REVIEW ARTICLE

Insomnia: An Overview

Mark J. Woyshville, Mansoor Ahmed
Cleveland Sleep Center, Faculty of Medicine & International Health
Case Western Reserve University-Cleveland, Ohio

Indian J Sleep Med 2006; 1.3, 125-130

Introduction

Now, blessings light on him that first invented sleep! It covers a man all over, thoughts and all, like a cloak; it is meat for the hungry, drink for the thirsty, heat for the cold, and cold for the hot. It is the current coin that purchases all the pleasures of the world cheap, and the balance that sets the king and the shepherd, the fool and the wise man, even. ~Miguel de Cervantes, Don Quixote, 1605.

Insomnia represents a spectrum of disturbances in which sleep is difficult to initiate, maintain, or is non-restorative. Insomnia is by far the most common and pervasive sleep problem, resulting in considerable morbidity including impaired daytime functioning, increased risk for psychiatric illness, and deterioration in the quality of life[1,2,3]. Risk factors for insomnia include increasing age[44] Mellinger G. D., Balter M. B., Uhlenhuth E. H. Insomnia and its treatment: prevalence and correlates, female sex[5], and physical or mental illness[6]. The economic burden of insomnia on individuals and society is huge, having been estimated at $15.4 billion[7].

Despite the fact that insomnia is pervasive (10% to almost 70% in primary care settings)[8,9] and results in significant morbidity and associated health care costs, the majority of insomnia sufferers remain undiagnosed and untreated[10]. This may be due to the fact that health care providers and the general public remain largely unaware about the nature, prevalence, and the impact of insomnia on health and health economics.

Address for Correspondence
Dr. Mansoor Ahmed
Medical Director SW-Cleveland Sleep Center
Faculty of Medicine & International Health
Case Western Reserve University-Cleveland, Ohio

Insomnia can be acute or chronic; it can be transient or persisting. A number of different nosological schemes exist for classifying the insomnias,[11,12,13] but in all cases that persist for more than a few days, insomnia symptoms are usually present at least three to four nights weekly. Insomnia is most often classified as either primary or secondary; in clinical practice, however, it is often difficult to differentiate the two due to substantial symptomatic overlap.

The biological mechanisms underlying insomnia are complex and involve homeostatic and circadian determinants of sleep and wakefulness. Furthermore, a host of external mitigating factors including medications, shift work, and chronic disease directly or indirectly influencing these mechanisms and thus the genesis and expression of insomnia. Indeed, insomnia is multifactorial in origin, involving predisposing, precipitating, and perpetuating factors.

This chapter provides a brief overview of insomnia, including definition, classification, prevalence, mechanisms, and therapeutics; it is not intended to be exhaustive but rather to suggest how one can recognize, evaluate, and manage insomnia in community settings.

Definition and Classification of Insomnia

A clinically useful definition of insomnia includes a description of sleep symptoms along with associated daytime complaints, as do the three major insomnia classification schemes (International Classification of Sleep Disorders (ICSD-2), Second Edition[11]; the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)[12]; and the International Classification of Diseases, Tenth Edition (ICD-10)[13]). Sleep symptoms usually include difficulty falling sleep

(sleep initiation) or staying asleep (sleep maintenance). Frequent nocturnal awakening after sleep onset and awakening in advance of the desired time constitute examples of sleep maintenance insomnia, and are over-represented amongst those with psychiatric disorders, particularly major affective syndromes.[12] In general, however, it is most convenient and clinically relevant to conceptualize in terms of comorbidity, duration and severity; although severity is necessarily convolved with frequency[14]:

- Comorbidity: Primary versus Secondary, such as insomnia due to the use of substances, a psychiatric illness, or a medical condition.
- Duration: Transient (2 to 3 days); Short-term (less than three weeks); and Long-term or Chronic (greater than three weeks).
- Severity: Mild (present almost nightly, but associated with little or no evidence of social or occupational impairment); Moderate (nightly symptoms with mild-to-moderate daytime impairment) and Severe (nightly symptoms with severe daytime impairment and distress, such as restlessness, fatigue, irritability, and anxiety.

As secondary insomnia is treated by addressing the causative comorbidity, which might itself be a primary sleep disorder (e.g., circadian misalignment syndromes), our focus will be on the primary insomnias, which the original International Classification of Sleep Disorders (ICSD)[15] organized into three categories:

- Psychophysiologic Insomnia (Learned insomnia, conditioned insomnia, functionally autonomous insomnia, psychophysiologic arousal, chronic somatized tension, internal arousal without psychopathology), whose essential feature is somatized tension and learned sleep-preventing associations that result in a complaint of insomnia and associated decreased functioning during wakefulness.
- Idiopathic Insomnia (Childhood-onset insomnia, lifelong insomnia, insomnia associated with problems within the sleep-wake system, excessive arousal, inadequately developed sleep system), whose essential feature is a lifelong inability to obtain adequate sleep, presumably due to an abnormality of the neurologic control of the sleep-wake system.
- Sleep State Misperception (Pseudoinsomnia, subjective complaint of disorder of initiation and maintenance of sleep without objective findings, insomnia without objective findings, sleep hypochondriasis, subjective complaint), whose essential feature is a complaint of insomnia (or excessive sleepiness) occurring without objective evidence of sleep disturbance.

Note that the first two categories share hyperarousal as a cardinal feature and indeed, hyperarousal is mechanistically implicated in the precipitation and perpetuation of most insomnias encountered in clinical practice; however, the third category, Sleep State Misperception, is a notable exception to this rule, the work-up of which is an exception to the general notion that polysomnography (sleep laboratory studies) are not useful in the diagnosis of insomnia[16].

Prevalence of Insomnia

Reported insomnia prevalence rates vary widely, reflecting the descriptive, methodological, and sample size differences amongst studies. Indeed, prevalence rates of 10% to almost 70% have been reported in primary care settings[8,9]. However, rates have dropped of late, reflecting the tendency towards greater specificity in the insomnia nosology. The current consensus is that about 30% of the general population complains of sleep disruption, while approximately 10% has associated symptoms of daytime functional impairment consistent with the diagnosis of insomnia[17].

When subpopulations are considered, differences in insomnia prevalence arise. For instance, insomnia complaints increase with age[4], although controlling for comorbities reveals that sleep changes little across adulthood[1818] Ohayon MM; Carskadon MA; Guilleminault C; Vitiello MV. Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: developing normative sleep values across the human lifespan. SLEEP 2004;27(7):1255-73 Although difficulty staying asleep is the most frequent insomnia symptom reported overall, youthful insomniacs are more prone to sleep initiation insomnia while elders are more likely to complain of sleep maintenance problems (middle and terminal insomnia)[19]. Women have more insomnia complaints than men; but the difference seems due to the increased prevalence of depressive and anxious comorbidities amongst women relative to men and indeed, there are no gender

differences on sleep[20]. Perimenopausal women constitute yet another subpopulation enriched for insomnia complaints, likely due in part to vasomotor instability[21,22,23,24]. Of course, medical morbidities of all kinds are associated with insomnia; in fact, chronic, severe insomnia confers as much quality-of-life morbidity as the serious medical comorbidities[25].

Finally, insomnia and psychiatric illness share a unique and profound relationship of reciprocal influence. Not only could up to 75% of insomniacs presenting to a sleep clinic could be given a psychiatric diagnosis[2626] Buysse DJ, Reynolds CF, Hauri PJ et al. Diagnostic concordance for DSM-IV sleep disorders: a report from the APA/NIMH DSM-IV field trial. Am J Psychiatry 1994;151(9):1351-1360, but persistent insomnia is a risk factor for the future development of psychiatric disorders[27,28,29,30,31,32]. Indeed, global insomnia is associated with completed suicide in major depression[33], and treating insomnia may prevent manic episodes in bipolar disorder[34].

Socio-economic Consequences of Insomnia

The medical morbidity of insomnia is costly; annual drug costs alone are estimated at $1.97 billion (prescription and over-the-counter), with the cost of providing direct services estimated at another $11.96 billion[35]. In addition there are "indirect" costs, such as those associated with:

- Increased (non-insomnia) health care costs[2,36]
- Increased absenteeism[1]
- Impaired daytime life-role performance[1,3]
- More accidents[3737] Balter MB, Uhlenhuth EH. New epidemiologic findings about insomnia and its treatment. J Clin Psychiatry 1992; 53[12, suppl.]: 34-9

Taken together, the directs costs of the medical morbidity of insomnia plus the fiscal burden of the "indirect" costs total an estimated $30 to $107.5 billion annually[38,39].

Mechanism of Insomnia

The search for a unitary hypothesis explaining insomnia in terms of observable biophysical parameters has succeeded in identifying hyperarousal as a candidate final common pathway for psychophysiologic and idiopathic insomnia. Evidence for hyperarousal amongst insomniacs includes the following:

- Hypermetabolism[3,40,41]
- Blunted heart rate variability as a function of sleep stage[42]
- Blunted serum cortisol circadian variability and increased total serum cortisol (AUC)[43,44]
- Lack of daytime sleepiness[4545] Sateia MJ, Doghramji K, Hauri PJ, Morin CM. Evaluation of chronic insomnia. An American Academy of Sleep Medicine review. SLEEP 2000;23:243-308

Normally, sleep pressure builds during the day, but wakefulness is maintained by the endogenous alerting signal from the circadian pacemaker in the hypothalamus (the suprachiasmatic nucleus). Towards evening, the circadian alerting signal ebbs, permitting the accumulated sleep pressure to drive sleep. Throughout the night the sleep pressure is gradually dissipated; towards morning the circadian alerting signal rallies and prompts awakening. Therefore, it could be reasoned that non-circadian alerting effect of hyperarousal militates against sleep, even when the circadian alerting signal is at its ebb and there is otherwise adequate sleep pressure, resulting in initial insomnia. Further, if the circadian alerting signal nadir (ebb) was delayed, sleep onset would be likewise be delayed; and indeed, there is evidence that core body temperature, a surrogate for the circadian nadir, is delayed in insomnia[46]. The mechanism of hyperarousal, however, seems insufficient in itself to explain middle and terminal insomnia; giving rise to speculation that pathology involving the circadian physiology of sleep might also be operative. Finally, there are those with chronic primary insomnia who show no evidence for hyperarousal when matched to controls in a constant routine[47].

Clinical Evaluation of the Insomnia Patient

The science of evaluating the insomnia patient has been perfected through extensive study and is largely formalized; the reader is referred to the excellent review by the American Academy of Sleep Medicine[45] for details. The *art* of evaluating the insomnia patient, however, defies formalization. Our experience has been that the key to making the most accurate diagnosis is to

obtain the best possible history, directed by a search for the predisposing, precipitating, and perpetuating factors pertinent to the manifest sleep complaint. As the insomnia patient rarely brings up the issue of a sleep disturbance without prompting; or worse, brings it up at the conclusion of the visit, a simple inquiry such as "How have you been sleeping lately?" made earlier rather than later in the interview, together with a receptive demeanor, will encourage a productive dialog. Pursuing the natural history of the sleep complaint from the patient's earliest recollections is critical, as the failure to do so is one of the chief reasons circadian rhythm disturbances are misdiagnosed as primary insomnia. Corroboration such as from a bed partner is very helpful if available; if not at the index interview, then subsequently. Finally, as the current severity of the patient's distress biases perception and recall congruently, gathering data longitudinally using a sleep diary will afford prospective diagnostic clarification; further, it will keep the patient engaged as a partner in the quest for diagnostic certainty and therapeutic efficacy. Should corroborated history, retrospectively and prospectively obtained, fail to clarify the diagnosis, a referral to a sleep specialist may be warranted.

The Therapeutics of Insomnia

The therapeutics of insomnia cleave at once into the pharmacologic and non-pharmacologic modalities. The pitfall of resorting to a pharmacologic intervention too early in the diagnostic process is that neither the diagnosis nor treatment will advance beyond the identification of target symptoms and their amelioration with medication. Ideally, medication serves the long-term goal of rehabilitating the patient's sleep through life changes which obviate the need for medication in the end; long-term medication without life changes, however, is the default position, seen more often than not in today's hectic, driven clinical milieu.

The single most readily identifiable and easily remedied factor in primary insomnia is sleep hygiene. Sleep hygiene instructions given along with a sleep diary at the initial visit is always appropriate for patients with an insomnia complaint. Good sleep hygiene includes:

- A dark, quiet, and serene sleep environment.
- Modest exercise in the afternoon or early evening – *not* at or near bedtime.
- Avoiding heavy meals late in the day.
- No alcohol after dinner.
- No nicotine after 4:00 P.M.
- No caffeine after 12:00 Noon.
- Arise at the same time of day, every day.
- No napping during the day.

Other non-pharmacologic approaches include the use of psychotherapeutic techniques to mobilize and modify unrealistic expectations of sleep, and to identify and rectify maladaptive sleep behaviors; engineering the sleep environment to be free of cues reinforcing the pairing of the sleep environment with insomnia – such as laying in bed when not sleepy or clock-watching ("stimulus control"); and setting a fixed time to arise each and every day, with no napping permitted – although bedtime itself is *ad lib* ("sleep restriction").

Finally, pharmacologic agents (hypnotics) play an important role in management of insomnia; they should be used for the short-term symptomatic management of insomnia symptoms pending the definitive rehabilitation of the sleep compliant. They should be prescribed judiciously, as the lowest effective dose for the shortest possible duration. The ideal hypnotic would have a rapid onset of action and sustained efficacy throughout the night, but confer no morning "hangover" nor daytime impairment of any kind; there should be neither tolerance nor withdrawal. The long-term safety and efficacy of hypnotics has not been established; indeed, if long-term treatment seems required, the diagnosis and treatment should be revisited, perhaps in consultation with a sleep specialist.

Conclusion

Insomnia is ultimately a complex, learned, conditioned behavior that, like cigarette smoking, can be difficult to rehabilitate. Therefore, the management of primary insomnia requires a *relationship* in which the patient is a partner with the physician in the service of self-mastery.

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