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Insomnia disorder: A review

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Abstract

Sleep problems are one of the most common complaints for adults in primary care. They are associated with a decline in overall health status and perception of poor health and can have negative personal and social consequences. The term insomnia is defined in different ways and can describe a symptom and/or a disorder. It involves dissatisfaction with sleep quantity or quality and is associated with one or more of the following subjective complaints like difficulty with sleep initiation, difficulty maintaining sleep, or early morning waking with inability to return to sleep. In DSM- V 'Insomnia Disorder' is described under the heading of 'Sleep-Wake Disorders'. It classifies insomnia under an umbrella term "insomnia disorders" where both primary and secondary insomnia are combined. In this paper the new and updated diagnostic criteria of Insomnia Disorder along with its etiology, pathophysiology and consequences will be discussed in detail.

Keywords: Insomnia disorder, DSM –V, sleep problem, sleep- wake disorder, primary insomnia, secondary insomnia

Introduction

Insomnia is derived from Latin word "insomnis" which is composed of "in" mean "not" and "somnus" means "sleep" which means no "sleep".

Sehar (Insomnia) is defined not simply by total sleep time but rather by difficulty in initiation and maintenance of sleep, poor quality of sleep and an insufficient duration of sleep, such that functioning in the awake state is impaired. Insomnia is the most prevalent sleep complaint, affects up to 10 to 59% of the adult population and is second only to the complaint of pain as a reason to seek medical attention ^[1].

Sleep problems are one of the most common complaints for adults in primary care ^[2]. They are associated with a decline in overall health status and perception of poor health and can have negative personal and social consequences ^[3].

The term insomnia is defined in different ways and can describe a symptom and/or a disorder. It involves dissatisfaction with sleep quantity or quality and is associated with one or more of the following subjective complaint(s): difficulty with sleep initiation, difficulty maintaining sleep, or early morning waking with inability to return to sleep ^[4].

Mental Health disorders are frequently associated with insomnia. An epidemiological study reports that individual with insomnia have 4.5 folds higher probability of presenting with depression compared with those with normal sleep pattern. In addition, patients with insomnia have an elevated risk of manifesting depression within 3.5 years after onset, even in absence of psychological disturbances ^[5]. Individuals with sleep problems also report higher levels of anxiety, physical pain and discomfort, and cognitive deficiencies ^[6]. Insomnia may be associated with long-term health consequences, including increased morbidity, respiratory disease, rheumatic disease, cardiovascular disease, cerebrovascular conditions, and diabetes ^[2, 6].

Classification of Insomnia

Insomnia is classified into three types on the basis of duration: (1) Transient Insomnia- in which symptoms last for <1 week, (2) Acute Insomnia- inability to consistently sleep well for 1–4 weeks/less than a month, and (3) Chronic Insomnia- in which symptoms are present for at least 3 nights/week for at least 1 month, and not be linked to other sleep, medical, or mental disorders ^[7, 8].

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Classification of sleep disorders based on DSM-5 criteria DSM-5, 2013, a diagnostic tool, has comparatively similar criteria to ICSD-3. It classifies insomnia under an umbrella term “insomnia disorders” where both primary and secondary insomnia are combined [4]. The publication of the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) fundamentally changed the landscape of sleep medicine and the diagnosis of insomnia. In DSM-IV, primary insomnia was distinguished from insomnia that is secondary to another diagnosis, including major depressive disorder and generalized anxiety disorder. DSM-IV understood secondary insomnia as a symptom of a primary psychiatric disease: the secondary insomnia was expected to normalize with treatment of the primary disorder [4].

Insomnia should be diagnosed using diagnostic criteria from the American Psychiatric Association's Diagnostic and Statistical Manual (DSM) and/or the International Classification of Sleep Disorders (ICSD). Both have been recently updated.

The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) describes it as ‘Insomnia Disorder’ under the heading of ‘Sleep-Wake Disorders’. In DSM- V, Insomnia disorder is characterized by poor sleep quality or quantity, including having difficulty falling asleep, remaining asleep, or returning to sleep after awakening and insomnia is experienced at least 3 nights per week for at least 3 months [9, 10].

DSM-V- Diagnostic Criteria for Insomnia Disorder:

Criteria I- VIII must be met

1. A predominant complaint of dissatisfaction with sleep quantity or quality, associated with one or more of the following symptoms:
 - a. Difficulty initiating sleep (in children, this may manifest as difficulty initiating sleep without a caregiver intervention).
 - b. The difficulty maintaining sleep, characterized by frequent awakenings or problems returning to sleep after awakenings (in children, this may manifest as difficulty returning to sleep without a caregiver intervention).
 - c. The early morning awakening with inability to return to sleep.
2. The sleep disturbance causes clinically significant distress or impairment in social, occupational, educational, academic, behavioural or other important areas of functioning.
3. The sleep difficulty occurs at least three nights per week.
4. The sleep difficulty is present for at least three months.
5. The sleep difficulty occurs despite adequate opportunity for sleep.
6. The insomnia is not better explained by and does not occur exclusively during the course of another sleep disorder (e.g., narcolepsy, a breathing related sleep

disorder, a circadian rhythm sleep-wake disorder, parasomnias).

7. The insomnia is not attributable to the psychological effects of a substance (e.g., drug abuse or a medication.)
8. Coexisting mental disorders and medical conditions do not adequately explain the predominant complaint of insomnia [4, 10, 11].

Etiology

There is no single cause of insomnia disorder but many factors may contribute to the onset of condition, including:

- a. **Stress and anxiety:** Stress or anxiety can cause tension or feelings of worry and overstimulation, which make sleeping difficult. Over time, the negative associations with sleeping may make it more difficult to fall asleep and stay asleep.
- b. **Mental disorders:** Approximately 80% of patients with psychiatric disorders describe sleep complaints. Depression and other mental disorders may contribute to the onset of insomnia disorder. Mood and hormonal changes can contribute to insomnia, while the reverse may also occur. In mania and Hypomania sleep latency is increased and total sleep time is reduced. Chronic alcoholic lack slow- wave sleep and decreased amount of REM sleep. Chronic schizophrenia also causes insomnia.
- c. **Medical Conditions:** There are several medical conditions are known to cause insomnia, such as rheumatologic disorders, use of glucocorticoids, chronic pain, nasal allergies, asthma, cardiac ischaemia, Paroxysmal nocturnal dyspnoea, COPD, cystic fibrosis, menopause, gastroesophageal reflux and thyroid dysfunctions may also cause discomfort and make it difficult to get to sleep or stay asleep.
- d. **Lifestyle factors:** Consumption of too much caffeine or alcohol can disturb the sleep patterns, while working from home or late at night can make winding down difficult. Daytime sleeping may also result in insomnia for some people.
- e. **Other Sleep Disorders:** Some sleep disorders may cause insomnia, or coexist with the condition. Restless leg syndrome, for example, can hamper attempts to sleep, while sleep apnoea causes the sufferer to wake briefly but repeatedly through the night.
- f. **Comorbidity:** Insomnia disorder may occur in isolation or comorbid with other conditions. Frequently, the disorder occurs with the subsequent physical disorders:
 - Diabetes
 - Coronary heart disease
 - Arthritis
 - Fibromyalgia
 - Chronic obstructive pulmonary disease

Moreover, insomnia disorder is often found to be comorbid with various mental disorders, including

- Bipolar disorder
- Anxiety disorder
- Depressive disorder [7, 12, 13, 14].

Table 1: The causes of insomnia may also be classified as follows

Medical Causes	Psychological Causes	Lifestyle Causes
<ul style="list-style-type: none"> • Nasal and sinus allergies • Gastrointestinal problems such as reflux • Endocrine problems such as hyperthyroidism • Arthritis • Asthma • Neurological conditions such as Parkinson's disease • Chronic pain • Low back pain • Sleep apnea • Prescription drugs such as antidepressants and medications for asthma or blood pressure also some pain medications, allergy and cold medications, and weight-loss products 	<ul style="list-style-type: none"> • Depression • Anxiety • Stress 	<ul style="list-style-type: none"> • Sedentary Lifestyle • Lack of exercise • Substance Abuse • Rotating shift work • Jet lag • Time zone change • Not getting enough exposure to sunlight • Drinking too much caffeine • Overheating a bedroom • Eating too much during dinner • Poor sleep habits • Stress

Source: Practo webpage

Pathophysiology

Insomnia is commonly conceptualized as a disorder of nocturnal and daytime hyper arousal, which is both a consequence and a cause of insomnia and is expressed at cognitive and emotional as well as physiological levels. Patients of insomnia disorder usually report excessive worry, racing thoughts, and selective attention to arousing stimuli. Hyper-arousal is manifested physiologically in those with insomnia as an increased whole body metabolic rate, elevations in cortisol level, increased whole-brain glucose consumption during both the waking and the sleeping states, and increased blood pressure and high-frequency electroencephalographic activity during sleep [15, 16].

Disruptions in the pattern and rhythm of REM and NREM sleep are frequently found when an individual admits to experiencing sleep disorders.

Sleep-wake cycles are governed by a complex group of biologic processes that serve as internal clocks. The supra-chiasmatic nucleus, presented in the hypothalamus, is considered to be the body's anatomic timekeeper, responsible for the release of melatonin on a 25-hour cycle. The pineal gland secretes less melatonin when exposed to bright light; thus, the level of melatonin is lowest during the daytime hours of wakefulness.

There are multiple neurotransmitters, which are considered to play role in sleep. These include serotonin from the dorsal raphe nucleus, norepinephrine contained in neurons with cell bodies in the locus ceruleus, and acetylcholine from the pontine reticular formation. On the contrary, the dopamine is associated with wakefulness.

Abnormalities in the delicate balance of all of these chemical messenger systems may disrupt various

physiologic, biologic, behavioural, and EEG parameters responsible for REM (i.e. active) sleep and NREM (slow-wave) sleep [17, 18].

Symptoms

- Inability to fall asleep
- Inability to continue/ maintain sleep
- Restless wakening after night sleep
- Sleepiness or tiredness during the day
- Burning sensation in eyes
- Irritability of moods
- Excessive thirst or dryness of mouth
- Drowsiness
- Fatigue
- Loss of memory
- Concentration problem
- Impulsiveness or aggression
- Lack of energy or motivation
- Errors or accidents [11].

Differential Diagnosis

Differential diagnosis of Insomnia Disorder is complex by signs and symptoms of other sleep disorders, especially obstructive sleep apnoea (OSA) or restless legs syndrome (RLS). These sleep disorders are not classified as insomnia disorder, but they are usually co-exist with symptoms of insomnia.

- **Obstructive sleep apnoea (OSA):** OSA includes breathing pauses during sleep and uncurbed daytime sleepiness. A complete sleep history should be taken, it can give understanding into these complaints, and diagnosis should to be confirmed by poly-somnography [19].

- **Restless legs syndrome (RLS):** RLS can be distinguished by four criteria suggested by the International RLS Study Group as follows: an urge to move the legs accompanied by unpleasant sensations, which is present at rest, which is relieved by movement and peaks at night or in the evening. The criteria can be evaluated by the Restless Legs Syndrome Rating Scale [20].
- **Circadian rhythm sleep disorder:** It is another common sleep disorder. This is marked by a disrupted internal sleep-wake clock, which results in disturbed sleep and daytime fatigue. The rhythm can be delayed, advanced or irregular [21, 22].

Management of Insomnia Disorder in Modern Medicine

A. Non-Pharmacological Treatment

Cognitive Behaviour Therapy: CBT is focused on treating insomnia (CBT-i), targets the maladaptive behaviour and thoughts that may have developed during insomnia or played a part in its development. CBT-i is thought to be the gold standard in the treatment of insomnia. CBT-i composed of five major constituents: stimulus control, sleep restriction (also known as sleep consolidation or bed restriction), relaxation techniques, cognitive therapy and sleep hygiene education.

1. **Stimulus control:** Stimulus control is a reconditioning treatment forcing distinction between daytime and sleeping environments [23]. For the patients of insomnia, the bedroom triggers associations with being awake and aroused. This treatment involves removing all stimuli that are possibly sleep-conflicting (reading, watching television and use of computers or mobile phone) and avoiding sleep from living areas. The patient is advised to get up if he or she is not able to sleep within 15–20 minutes, or when wakeful during the night or feeling increasing distress, and not return to bed until feeling sleepy.
2. **Sleep-restriction therapy:** Sleep restriction sympathizes to better matching the time spent in bed to the average night sleep duration [24]. Patients are advised to keep a sleep diary to ascertain average sleep duration. They are then advised to spend a period of time in bed equal to this plus 30 minutes, and set a regular time to arise. Some patients can perceive the amount of sleep lesser, but, the time in bed should never be set at less than 5 hours. When sleep becomes stronger, the length of time in bed can be moderately increased in 15–30 minute increments. This therapy induces natural sleepiness (reduced time in bed) and gives a sense of assurance to the patient, that bed is now a safe place to sleep.
3. **Relaxation techniques:** This include progressive relaxation, imagery training, biofeedback, meditation, hypnosis and autogenic training. Patients are advised to practice relaxation techniques all over the day and early evening. Even it is useful a few minutes two to four times a day. A last minute relaxation attempt done few minutes before going to bed, will not work. Muscular tension and cognitive arousal (e.g. a “chattering” mind) are contradictory to sleep. These techniques may act by distraction at the cognitive level. Relaxation lowers physical and mental arousal but is less efficacious as alone treatment and is better used in combination with other treatments.

4. **Cognitive therapy:** It involves enabling the patient to acknowledge, how disposed and negative thinking about sleep increases physiological and psychological arousal levels. Sitting aside 15–20 minutes in the early part of the evening to write down any worries, make plans for the next day and label any anxiety that may arise during the night allows the day to be put to rest. Thought-stopping efforts or blocking techniques, such as repeating any word every 3 seconds, occupy the short-term memory store, which allows the sleep to establish. Cognitive restructuring confronts unhelpful beliefs, such as “if I don’t get enough sleep tonight, tomorrow is going to be a bed day”, which maintain both wakefulness and helplessness. Another cognitive and behavioural technique is paradoxical intention. Patients are advised to put the effort into stay awake rather than trying to fall asleep (DE catastrophizing), it strengthens the sleep drive and reduces performance effort [25].

5. **Sleep hygiene education:** This is a general guidelines given to the patients about healthy sleep behaviours and a healthy sleep environment. It emphasises environmental factors, physiological factors, behaviour, habits that promote sound sleep. One of the most important sleep hygiene practices is to proper amount of time asleep spend.

- Long naps in daytime should be avoided-Limiting daytime naps to 30 minutes.
- Exercise to promote good quality of sleep. At least 10 minutes of aerobic exercise, such as walking or cycling, can improve sleep quality during night.
- Simulants such as caffeine and nicotine close to bedtime should be avoided.
- Alcohol intake should be avoided, especially before bed.
- Visual access to clock should be avoided, when in bed.
- Sleep environment should be pleasant. Bedroom should be dark, quiet and clean. Mattress and pillows should be comfortable. Bright light from lamps, cell phone and TV screens should be turned off [26, 27].

B. Pharmacological Treatment

Benzodiazepines: It include long-acting forms (eg, flurazepam, quazepam), intermediate-acting forms (eg, temazepam, estazolam), and short-acting forms (triazolam). The long-acting agents are seldomly used today for insomnia due to daytime sedation, cognitive impairment, and increased risk of falls in elderly patients. They were commonly used until the 1980s, when tolerance, dependency, and daytime side effects were not recognized as major limitations of these agents. Temazepam is still used for a short-term course (from days to 1-2 weeks), at a dose of 15-30 mg at bedtime [28].

Sedative-hypnotic drugs

Sedative-hypnotic medications do not cure insomnia, but they can provide symptomatic relief as sole therapy or as a supplement with CBT. Moreover, some patients cannot stick fast to or do not respond to CBT, in that condition these agents are used. The non-benzodiazepine receptor agonists (eg, eszopiclone, zolpidem, zaleplon) are thought to be less habit-forming than benzodiazepines and, for that reason, are

important for long-term treatment of chronic insomnia. The most suitable use of non-benzodiazepine receptor agonists is for transient and short-term insomnia in combination with non-pharmacologic treatment [28].

Suvorexant

Suvorexant (Belsomra) is the first orexin receptor antagonist for insomnia and was approved by the FDA in August 2014. It is indicated for the treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance [28]. The American Academy of Sleep Medicine (AASM) recommended, the use of suvorexant for the treatment of insomnia as opposed to no treatment (Sateia MJ, 2017). The orexin neuropeptide is a central promoter of wakefulness, which blocks the binding of wake-promoting neuropeptides named as orexin A and orexin B to receptors OX1R and OX2R. Suvorexant is considered to suppress wake drive [28].

Sedating Antidepressants

In spite of the fact that, there is a scarcity of clinical data on the use of sedating antidepressants for the treatment of insomnia without mood disorders, these agents are still sometimes used. Sedative tricyclic antidepressants, like amitriptyline, nortriptyline, and doxepin, and the tetracyclic drug mirtazapine have been used. Tricyclic drugs and mirtazapine can bring out daytime sedation, weight gain, dry mouth, postural hypotension, and cardiac arrhythmias. Trazodone can cause priapism in men, daytime sedation, and hypotension [28].

Antihistamines

Antihistamines are the prime constituent of over-the-counter (OTC) sleep aids and are also the ingredient in cold and sinus medicines, which are sold as bedtime-use medications. However, common antihistamines (i.e. first-generation H1-receptor antagonists such as diphenhydramine, hydroxyzine, and doxylamine) are not indicated for the treatment of insomnia [28].

While H1 antihistamines have sedative effects in healthy persons, no study has done to reveal an effective dose range for patients with insomnia. These medicines may have some subjective benefit, but long-term efficacy and safety have not been explained. Thus, regular use of these medicines in insomnia patients is not advised [29].

Melatonin

Melatonin is a hormone, which is secreted by the pineal gland. Its concentration in the blood is highest during normal times of sleep and lowest during normal times of wakefulness. It is considered that melatonin given during normal waking hours has hypnotic effects.

However, administration in the evening time, is critical as to whether a hypnotic or chronobiologic effect occurs. When Melatonin is given early in the evening, it is considered to increase sleep time; however, its administration 30 minutes before a normal bedtime has not result in a decreased sleep latency or an increase in sleep time [28]. There are evidences, to suggest that melatonin taken before bedtime decreases sleep latency and may increase total sleep time [30].

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