GUIDELINES FOR THE TREATMENT OF SLEEP DISORDERS

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INTRODUCTION

Disturbed sleep is among the most frequent health complaints physicians encounter. For most, it is an occasional night of poor sleep or daytime sleepiness. However, at least 15%-20% of adults report chronic sleep disturbance or misalignment of circadian timing. These lead to serious impairment of daytime functioning and may contribute to exacerbate medical psychiatric conditions.

Clinical psychiatrists and psychologists of the new millennium will need to master general basic knowledge of sleep and chronobiology, the disorders of sleep and circadian rhythms, and their clinical management (1,2).

Disordered sleep has protean effects on mood, attention, memory and general sense of vigor. Furthermore, disturbance in sleep has clear prognostic value and must be addressed to optimize clinical come.

DIAGNOSTIC CATEGORIES

Sleep Disorders

Sleep disorder can be divided into four major categories:

1. Dyssomnias: disorders associated with complaints of insufficient, disturbed, or non-restorative sleep.
3. Disturbances of the circadian sleep-wake cycle.
4. Parasomnias: abnormal behaviors or abnormal physiological events in sleep (1, 2).

By the definition, the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) limits itself to chronic disorder (at least 1 month in duration) (1). On the other hand, the International Classification of Sleep Disorders includes sleep disorder of short-term and intermediate duration, which in fact are more common than chronic disorders (3).

Primary sleep disorders result from conditions inherent to the mechanism by which sleep is regulated. Sleep may be disturbed owing to pain or discomfort from medical illness, considered in term of DSM-IV-TR to be secondary sleep disorders. In addition, sleep disorders may be related to other mental disorders, general medical conditions, and substance abuse.

Following are the diagnostic criteria for the different categories:

DYSSOMNIAS:

1. Primary Insomnia: DSM IV TR classification
   a. The predominant complaint is difficulty initiating or maintaining sleep, or non-restorative sleep, for at least 1 month.
b. The sleep disturbance (or associated daytime fatigue) causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

c. The sleep disturbance does not occur exclusively during the course of narcolepsy, breathing-related sleep disorder, circadian rhythm sleep disorder, or a parasomnia.

d. The sleep disturbance does not occur exclusively during the course of another mental disorder (e.g., major depressive disorder, generalized anxiety disorder, a delirium).

e. The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

2. Primary Hypersomnia: DSM IV TR classification

a. The predominant complaint is excessive sleepiness for at least 1 month (or less if recurrent) as evidenced by either prolonged sleep episodes or daytime sleep episodes that occur almost daily.

b. The excessive sleepiness cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

c. The excessive sleepiness is not better accounted for by insomnia and does not occur exclusively during the course of another sleep disorder (e.g., narcolepsy, breathing-related sleep disorder, circadian rhythm sleep disorder, or a parasomnia) and cannot be accounted for by an inadequate amount of sleep.

d. The disturbance does not occur exclusively during the course of another mental disorder.

e. The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

Specify if:

Recurrent: If there are periods of excessive sleepiness that last at least 3 days occurring several times a year for at least 2 years.

3. Narcolepsy: DSM IV TR classification

a. Irresistible attacks of unrefreshing sleep that occurs daily for at least 3 months.

b. The presence of one or both of the following:
   1. Cataplexy (i.e., brief episodes of sudden bilateral loss of muscle tone, most often in association with intense emotion)
   2. Recurrent intrusions of elements of REM sleep into the transition between the sleep and wakefulness, as manifested by either hypnopompic or hypnagogic hallucinations or sleep paralysis at the beginning or end of sleep episodes.

c. The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or another general medical condition.

4. Breathing-Related Sleep Disorder: DSM IV TR classification

a. Sleep disruption, leading to excessive sleepiness or insomnia that is judged to be due to a sleep-related breathing condition (e.g., obstructive or central sleep apnea syndrome or central alveolar hyperventilation syndrome).
b. The disturbance is not better accounted for by another mental disorder and is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or another general medical condition (other than breathing-related disorder).

5. Circadian Rhythm Sleep Disorder: DSM IV TR classification
   a. A persistent or recurrent pattern of sleep disruption leading to excessive sleepiness or insomnia that is due to a mismatch between the sleep-wake schedule required by a person’s environment and his or her circadian sleep-wake pattern.
   b. The sleep disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
   c. The disturbance does not occur exclusively during the course of another sleep disorder or other mental disorder.
   d. The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

Specify type:

- **Delayed sleep phase type**: a persistent pattern of late sleep onset and late awakening times, with an inability to fall asleep and awaken at a desired earlier time.

- **Jet lag type**: sleepiness and alertness that occur at an inappropriate time of day relative to local time, occurring after repeated travel across more than one time zone.

- **Shift work type**: insomnia during the major sleep period or excessive sleepiness during the major awake period associated with night shift work or frequently changing shift work.

- **Unspecified type**

6. Periodic Limb Movements in Sleep (PLMS) Previously called nocturnal myoclonus, is a disorder in which repetitive, brief, and stereotyped limb movements occur during sleep, usually about every 20 to 40 seconds. It has following features
   - Leg kicks every 20-40s
   - Duration of 0.5-5s
   - Complaints of:
     - Insomnia
     - Excessive sleepiness
     - Restless leg
     - Very cold or hot feet
     - Uncomfortable sensations in legs

**PARASOMNIAS:**

The parasomnias are a group of disorders characterized by disturbance of either physiological processes or behavior associated with sleep, but not necessarily causing disturbances of sleep or wakefulness. It includes:

1. **Nightmare Disorder (DSM-IV-TR criteria)**
   a. Repeated awakenings from the major sleep period or naps with detailed recall or extended and extremely frightening dreams, usually involving threats to survival, security, or self-esteem. The awakenings generally occur during the second half of the sleep period.

(234)
b. On awakening from the frightening dreams, the person rapidly becomes oriented and alert (in contrast to the confusion and disorientation seen in sleep terror disorder and some forms of epilepsy).

c. The dream experience, or the sleep disturbance resulting from the awaking, causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

d. The nightmares do not occur exclusively during the course of another mental disorder (e.g., a delirium, posttraumatic stress disorder) and are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

2. **Sleep Terror Disorder (DSM-IV-TR criteria)**

   Recurrent episodes of abrupt awakening from sleep, usually occurring during the first third of the major sleep episodes and beginning with a panicky scream.

   b. Intense fear and signs of autonomic arousal, such as tachycardia, rapid breathing, and sweating, during each episode.

   c. Relative unresponsiveness to efforts of other to comfort the person during the episode.

   d. No detailed dream is recalled and there is amnesia for the episode.

   e. The episode cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

   f. The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

3. **Sleepwalking Disorder (DSM-IV-TR criteria)**

   a. Repeated episodes of rising from bed during sleep and walking about, usually occurring during the first third of the major sleep episode.

   b. While sleepwalking, the person has a blank, staring face, is relatively unresponsive to the efforts of others to communicate with him or her, and can be awakened only with great difficulty.

   c. On awakening (either from the sleepwalking episode or the next morning), the person has amnesia for the episode.

   d. Within several minutes after awakening from the sleepwalking episode, there is no impairment of mental activity or behavior (although there may initially be a short period of confusion or disorientation).

   e. The sleepwalking causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

   f. The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

4. **REM Sleep Behavior Disorder**

   It is associated with complicated behaviors during sleep such as walking, running, singing and talking (4). It occurs during second half of night during REM sleep.

   (235)
5. Sleep Disturbance related to Other Psychiatric Disorder

6. Sleep Disorder in other Medical Condition

7. Substance-Induced Sleep Disorder

REVIEW OF MANAGEMENT OF INSOMNIA

NON-PHARMACOLOGICAL MANAGEMENT

Most insomnia patients indicate that they would prefer a non-pharmacologic solution to their insomnia (5). There are several effective treatment approaches to chronic insomnia that do not involve the use of hypnotics (6). Education about normal sleep and counseling around habits for promoting good sleep hygiene are a good but insufficient intervention when used alone (7, 8). Various relaxation therapies hypnosis, meditation, deep breathing, and progressive muscle relaxation can be helpful. These techniques in contrast to use of hypnotics, are not immediately beneficial but require several weeks of practice to improve sleep (9). Success is dependent on high degree of motivation in patients, who must devote considerable time to practice these techniques. Those who succeed in learning these techniques have a greater satisfaction with maintenance treatment than do patients chronically using hypnotics (10, 5). Furthermore, responders to behavioral interventions have sustained benefits after 6 months (11). Biofeedback can be helpful in those patients who are not sensitive to their internal state of arousal (12). Patients are provided an external measure of a biological variable such as an EMG or EEG that allows them a means to influence their own level of arousal. Sleep restriction therapy is similarly aimed at reducing the amount of wake time spent in bed (13).

Cognitive Behavior Therapy (CBT)

Morin et al, 1993 (14) found the CBT was effective in reducing sleep latency, waking up, early morning awakening and increasing sleep efficiency. Morin et al 1999 (15) found both CBT and pharmacotherapy effective for short term management of insomnia but that improvement was better sustained over time with CBT.

Behavioral treatments, in combination with addressing sleep hygiene, may be helpful in treating psycho physiological and other insomnias. Relaxation training (progressive relaxation, autogenic training, meditation, deep breathing) can all be effective if over taught to become automatic. Two other behavioral therapies have been shown to be effective: Stimulus control and Sleep restriction therapy (16, 13, 8) both requiring more than 3 weeks to be effective.

Stimulus Control: Stimulus control behavioral modification focuses on eliminating environmental cues associated with arousal (and aims to break the negative association of being in bed unable to sleep (10). The goal is to remove all behaviors from bedroom except sleep and loving.

Sleep restriction Therapy is similarly aimed at reducing the amount of wake time spent in bed (13) and is based on the observation that more time spent in bed leads to fragmented sleep.

CBT emphasizes the role of dysfunctional thoughts in maintenance of primary insomnia. Not only it is known to improve sleep efficiency but also has been demonstrated to aid in BZD discontinuation in older insomnia. It also imparts a greater sense of control over the problems. One may use systematic desensitization by reciprocal inhibition aiming to desensitize the patients to the associated experience. Other techniques, each with minimal efficacy are somatic relaxation, including muscle relaxation procedures, Electromyographic biofeedback, paradoxical intention, cognitive focusing.
A comprehensive review of the efficacy of non-pharmacological treatment for chronic insomnia, based on two meta-analysis and 48 individual treatment studies, showed reliable improvement in the main outcome measures of latency to sleep and wake time after sleep onset. Data consistently indicated that 70%-80% of insomnias benefited from the treatment. Sleep latency was reduced and subjective report of sleep quantity and quality improved. Improvements with behavioral treatments are well maintained over at least 6 months.

Relaxation and biofeedback therapies

Relaxation techniques target the cognitive or physiological arousal that interferes with sleep. A number of relaxation therapies have been used for insomnia, including PMR and biofeedback to diminish physiologic arousal, and imagery techniques, autogenic training, and meditation to reduce cognitive arousal. Relaxation techniques may be most useful for sleep onset insomnia. In general, the magnitude of improvements seen with relaxation is smaller than for other behavioral approaches.

PHARMACOLOGICAL TREATMENTS FOR INSOMNIA

Several medication classes are used for the treatment of insomnia, although the strength of evidence regarding their efficacy and tolerability varies considerably. A wide variety of sedating medication has commonly been used as sleeping pills, which vary in pharmacokinetic properties and side effects.

The ideal sleeping pill would shorten latency to sleep, maintain normal physiological sleep all night without blocking normal behavioral responses, leave neither hangover nor withdrawal effects the next day; be devoid of tolerance and side effects such as Impairment of breathing, cognition, and coordination, and should not be habit forming or addictive.

Short life hypnotics usually produce less daytime sedation than those with longer half-life drugs, but they often result in more rebound insomnia when they are discontinued. However, they relatively cause more amnesia especially for material that is learned during the period of peak concentration of drugs.

The major classes are benzodiazepine receptors agonists (BzRAs), antidepressant drugs (AD), antihistamines, melatonin, and various herbal remedies including valerian root extracts. Of these medications, only BzRAs are formally approved for the indication of insomnia treatment in the United States.

Benzodiazepine Receptor Agonists

Benzodiazepine receptor agonists (BzRAs) include the true benzodiazepines (e.g., triazolam, temazepam, estazolam, and lorazepam) as well as a structurally dissimilar group of nonbenzodiazepine agents, including an imidazopyridine (zolpidem), pyrazolopyrimidine (zaleplon), and cyclopyrolone (zopiclone). BzRAs are the only pharmacologic agents currently approved by the FDA for the treatment of insomnia, and they are labeled for short-term use (i.e., less than 4 weeks).

In summary, these agents bind at a specific recognition site in the benzodiazepine-α-aminobutyric acid (GABA)-chloride ion channel macromolecular complex. This binding is responsible for the hypnotic, anxiolytic, myorelaxant, and anticonvulsants actions of BzRAs.

There is some evidence that the nonbenzodiazepine BzRAs, specifically zolpidem, may be relatively more specific for hypnotic effects relative to anticonvulsants and anxiolytic effects: this may be related to greater specificity for benzodiazepine type 1 receptors.
Specific BzRAs differ significantly in pharmacokinetic properties, including the rate of absorption, extent of distribution, and rate of elimination. BzRAs also range widely in elimination half-life, from 1 hour for zaleplon to 120 hours for flurazepam and its metabolites. Finally, these agents differ in terms of active metabolites, which may have longer half-lives than the parent compound.

BzRAs are efficacious in the short-term treatment of insomnia. Recent metaanalyses examined BzRAs effects on sleep latency, sleep duration, number of awakenings, and sleep quality (21,22). For each of these outcomes, the effect size ranged between 0.55 and 0.75, substantiating the superiority of these agents over placebo. Other data support a broader range of beneficial outcomes. For instance, treatment with zopiclone for both 14 days and 8 weeks of treatment was associated with greater improvements in quality of life measures, social activities and professional activities compared to placebo (23). A survey of patients with untreated insomnia and those receiving benzodiazepines showed that the later group reported fewer symptoms of feeling blue, down in the dumps, or depressed, and being easily upset compared to the former group (24).

BzRAs have consistent effects on polysomnography (PSG) sleep measures (25). As expected, BzRAs are associated with reduced sleep latency and wakefulness during the night, and increased sleep duration and sleep quality ratings. Other specific PSG effects depend on the particular agent. For instance, zaleplon, with its very short half-life, has not been demonstrated to consistently affect sleep duration despite its effect on sleep latency. Traditional benzodiazepines reduce REM and stages 3 to 4 NREM sleep, whereas zaleplon and zolpidem are not associated with changes in sleep stages. In addition, BzRAs reduce the number of periodic limb movements and arousals associated with these movements (26). BzRAs can also lead to oxyhemoglobin desaturations during sleep and can theoretically worsen sleep apnea; however, in patients with moderate degrees of sleep apnea, the change in number of apneas and oxyhemoglobin saturation is felt to be clinically insignificant (27).

Although BzRAs have been studied primarily for short-term treatment of insomnia, insomnia is often a chronic condition, and many patient take their hypnotics for longer periods of time. Some patients clearly developed tolerance with continued use of BzRAs, and some polysomnographic (PSG) studies support this phenomenon (28); however, other PSG studies show continued efficacy over several nights of continued nightly administration. For instance, trizolam, zolpidem, and zaleplon have shown continued efficacy over a period of 4 to 5 weeks in double-blind, placebo controlled studies (29-32), and single blind studies have shown continued efficacy by PSG for as long as 6 months (33,34). Studies using self-ratings or observer ratings have documented efficacy for even longer amounts of time. For instance, double-blind studies have shown continued efficacy for up to 24 weeks with no evidence of tolerance according to mean subject rating (35,36) and single blind studies have shown efficacy for up to 1 year of treatment (37,38); however the role of BzRAs in long-term treatment or maintenance treatment of insomnia remains to be more clearly defined.

BzRAs can have significant adverse effects. The most common of these is a continuation of their desired therapeutic effects, sedation during the daytime. Daytime sleepiness is clearly more severe with longer-acting agent such as flurazepam, which has been documented in PSG studies (29, 39). Similar PSG studies of short-acting hypnotics have not shown an increase in daytime sleepiness. BzRAs are also associated with dose-related anterograde amnesia that may even be primarily responsible for their therapeutic affect (40, 41). BzRAs can also impair other aspects of psychomotor performance including reaction time, recall, and vigilance. Whether or not such deficits improve with discontinuation of the drug is more controversial, with some studies noting improvement following discontinuation (42, 43) and other studies failing to show such improvement (44).
BzRAs are significantly related to an increased risk of injurious falls and hip fractures in elderly people. In particular, risk seems to be increased with the use long-acting agents, high doses, multiple agents, and cognitive impairments in patients (45, 46).

Several discontinuation phenomena have been examined in relation to BzRAs. Rebound insomnia refers to an increase in insomnia symptoms beyond their baseline levels. Rebound is thought to be associated primarily with short-acting BzRAs, although recent evidence for zolpidem and zaleplon does not show the effect. Patients who demonstrate rebound insomnia tend to have worse baseline sleep and higher medication doses than patient without rebound (47, 48). The behavioral aspect of taking a pill may contribute to rebound insomnia. Individuals who have shown a poor response to treatment may show the greatest rebound (49). Withdrawal symptoms may occur in 40% to 100% of patients treated chronically with benzodiazepines, and can persist for days or weeks following discontinuation (50, 51). Withdrawal symptoms can include dizziness, confusion, depression, and feeling of unreality. Cognitive and behavioral treatments can help patients discontinue chronic benzodiazepine use (52). The prevalence of true withdrawal phenomenon in any individual treated with one-daily hypnotic dose of BzRAs is not well known. Recurrence is another potential discontinuance syndrome that has received little attention in insomnia. Given that insomnia tends to be chronic, it should not be surprising that many patients complained of their original symptom after discontinuation of an effective treatment. The role of recurrence in chronic BzRAs treatment also remains to be well defined. Finally, abuse of BzRAs used for insomnia appears to be uncommon. One survey showed no greater use of increased doses for BzRAs compared to antidepressants (53).

Antidepressant Drugs

Although use of antidepressant drugs (AD) for insomnia has increased dramatically, evidence to support their efficacy is relatively sparse. The most commonly used ADs for insomnia include trazodone, tertiary tricyclic agents, and mirtazapine. These drugs clearly have diverse effects on neurotransmission. In general, the sedating properties of antidepressants are related to antagonism of serotonin 5-HT2, histamine, and α1-adrenergic receptors.

Antidepressant drugs vary widely in their effects on sleep continuity, EEG data activity and slow-wave sleep, and REM sleep. Sleep continuity effects are likely to be most important in the treatment of insomnia. Some antidepressant drugs also can cause or exacerbate insomnia problems. Selective serotonin reuptake inhibitors (SSRIs) bupropion, noradrenergic selective tricyclic drugs and strongly serotonergic tricyclic drugs (e.g., clomipramine) are the most common agents to have such effects. In addition, serotonergic specific antidepressants can lead to anomalous sleep stages characterized by eye movements during NREM sleep and they can also cause or exacerbate restless leg syndrome and periodic limb movements. Antidepressants may also be associated with slight improvements in sleep apnea (57).
Studies with small number of subjects and diverse inclusion criteria suggested the beneficial effects of trazodone 150 to 400 mg on sleep continuity measures, as well as a tendency to increase stages 3 to 4 sleep and improve subjective sleep quality ratings, in insomnia patients (58-60). A more recent 2-week double-blind placebo-controlled study compared the effects of trazodone 50 mg and zolpidem 10mg to placebo among individuals with primary insomnia (61). This study showed improvements in subjective sleep latency and sleep duration with both active drugs although there was some evidence for superiority of zolpidem during the second treatment week. Both drugs were well tolerated. Other studies involving primary insomnia have shown beneficial effects of short-term treatment with low-dose doxepine (62) and trimipramine (63) compared to placebo. Finally, a recent open-label trial of paroxetine for primary insomnia in the elderly showed significant improvement in a multivariate measures of sleep quantity based on both diary and polysomnographic sleep measures (64). Small improvements were noted in diary-based measures of sleep quality and PSG measures of sleep efficiency; however, the greatest improvements were noted in daytime symptoms of mood and well being. Thus, it may not simply be the sedating properties of antidepressants that lead to improvement in insomnia.

Indirect evidence for the efficacy of antidepressants, and differential effects among agents, comes from studies in individuals with major depression. For instance, fluvoxamine has a relatively alerting effect relative to desipramine that in turn is more alerting than amitriptyline (65, 66). A comparison of trimipramine and imipramine found that both drugs improve sleep quality, although trimipramine was associated with more positive effects on PSG sleep (67). A comparison of fluoxetine with trazodone showed that the latter drug was not only associated with more improvements in insomnia symptoms, but also with a greater percentage of sedating events during the daytime (68). A series of comparison between fluoxetine and nefazodone has consistently shown that both drugs improve subjective sleep quality among depressed patients, although the change appears to be larger with nefazodone (69, 70). Nefazodone also led to improvements in PSG sleep efficiency, whereas fluoxetine was associated with mild decrements.

Antihistamines

Antihistamines such as diphenhydramine are among the most widely available over-the-counter preparations for insomnia. The mechanism of action of these drugs involves inhibition of histamine H1 receptors. Histaminic neurons in the posterior hypothalamus promote wakefulness through interaction with ascending cholinergic nuclei. Inhibition of H1 receptors leads to decreased alertness and subjective sedation. The elimination half-life of diphenhydramine range from 3 to 5 hours, within increase in elderly persons. In addition to their effect on histamine, these medications can also have antimuscarinic anticholinergic effects.

Despite their widespread use, a large body of well-documented research does not support the efficacy of antihistamines (71). Diphenhydramine 50 mg, improved subjective rating of sleep quality, sleep time, sleep latency, and wakefulness after sleep onset in middle-aged subjects with insomnia (71). A more recent study comparing the effects of lorazepam versus a combination of lorazepam plus diphenhydramine showed a slight advantage for the combination preparation in terms of sleep latency and subjective sleep quality (72). On most sleep measures, the two drug preparation were fairly similar. Studies of antihistamines in elderly people demonstrate subjective sedative properties comparable in magnitude to those of benzodiazepines and confirmed by effects such as increased sleep time, decreased awakening, and shorter sleep latency (73, 74).
Adverse effects of antihistamines include a range of cognitive and performance impairments (75). The anticholinergic effects of these medications may be of particular concern in elderly subjects. The relative safety and efficacy of antihistamine with more sustained use has not been examined.

**Melatonin**

Melatonin has been widely used as a "natural" sleep promoting agent. Data regarding its efficacy and safety have been mixed. The study designs, doses, and outcome measures used in melatonin trials have been quite variable and may contribute to inconsistent findings (76). Melatonin is secreted by the pineal gland during hours of darkness and the secretion of melatonin may result from influence of specific receptors in the suprachiasmatic nucleus of the hypothalamus (77). In addition, melatonin shifts circadian rhythms according to phase response curve (78, 79). The half-life of endogenous melatonin is less than 1 hour. Exogenous melatonin is absorbed from the gastrointestinal tract. A wide variety of preparations are commercially available, ranging from very short-acting to very long-acting agents, with half-lives ranging from several minutes to approximately 8 hours. Doses greater than 1 mg are likely to include supraphysiological concentrations. Clinical trials have employed doses ranging from 0.1 to 80 mg.

During daytime administration, melatonin causes sleepiness and fatigue and in healthy subjects (80, 81). When administered in night to healthy subjects, melatonin decreases sleep latency (82) and the number of awakenings, and improves sleep efficiency in an experimental insomnia paradigm (83). Studies in insomnia patients have also yielded inconsistent findings. Single night administration seems to produce very little effects (84). Subjective sleep ratings showed no effects in another trial of 5 mg for 1 week (85), whereas a 14-day trial of 75 mg resulted in increased subjective sleep time (86). Trials of melatonin in elderly people have ranged from 1 to 21 days. The most consistent effect is reduced sleep latency with some evidence as well for reduced nighttime wakefulness using sustained-released preparations (87-90). In a carefully designed 14-days crossover trial, immediate- and sustained-release melatonin were associated with shortened sleep latency, but no change in sleep time, sleep efficiency, wakefulness, or subjective sleep measures (91).

Adverse effects associated with melatonin have not been carefully evaluated. Melatonin affects reproductive cycles in several mammalian species, and reports have indicated the potential for worsening of sleep apnea and impaired cognitive and psychomotor performance during daytime administration. There are also some concerns regarding vasoconstriction as a potential side effect.

**Valerian Extract**

Valerian extract is one of the most widely used herbal remedies for insomnia. These extracts are derived from roots of the genus Valeriana, most often of the species *V. officinalis*. They contain a number of potentially active compounds, including sesquiterpenes and valepotriates. Valerian extracts show affinity for GABAA receptors, which may be related to the high amount of GABA itself that is often contained in these preparations (92, 93). However, GABA does not cross the blood-brain barrier, so this is an unlikely mechanism of action. Other potential actions include affinity for serotonin and adenosine receptors. Clinical studies with valerian extracts show mild sedative and anxiolytic effects. In particular, four double-blind placebo-controlled studies have examined doses of 400 to 900 mg of valerian extract over periods of time from 1 to 8 days, and in diverse subject populations ranging from healthy young adults to elderly insomniacs (94-97). Subjective effects include decreased sleep latency and improved sleep quality (94, 96, 97). One study also reported decreased subjectively
rated awakenings (94). Polysomnographic studies have shown an increase in stage 3 to 4 NREM sleep and reduced stage 1 sleep (95), with no change in sleep onset time, awake time after sleep onset, or other measures of sleep continuity (95,96). Likewise, valerian was found not to influence the EEG power spectrum during sleep (96). Small numbers of subjects, different inclusion criteria, and inconsistent findings hamper findings from these studies. These studies do not demonstrate the efficacy of valerian extract in most groups of individuals with primary insomnia.

Clinical studies have suggested a generally favorable side effect profile for valerian extract; however, the sedative effects of valerian may potentiate the effects of other CNS antidepressants (93).

Combination- Non pharmacological and Pharmacological treatment

In a randomized controlled trial conducted by Morin et al 1999(17) patients receiving cognitive behavior therapy (CBT) alone or CBT with temazepam rated themselves as significantly less impaired than those receiving drug treatment alone or placebos. They concluded that drug therapy gradually lost its clinical benefits over time but behavioral therapy had more lasting effects. Kupfer and Reynolds 1997 (98) in a review article stated that to achieve treatment goals for patients with insomnia, educational, behavioral and pharmacologic interventions should be combined. Attarian 2000 (100) concurred with this statement when he noted that the best management for insomnia is a combination of hypnotic medication and behavioral methods. Holbrook et al 2000 (101) also advocates a three step approach to treatment in primary care: (i) look for reversible underlying causes; (ii) non-pharmacological therapy; and (iii) pharmacological therapy. An earlier article by Rajput and Bromley in 1999 (102) stated the following:

• drug therapy may be beneficial for short-term improvement
• behavioral intervention may produce more sustained effects
• behavioral intervention combined with pharmacologic agents may be more effective than either approach alone.

Wohlgemuth et al 2001 (103) after conducting a randomized controlled trial comparing CBT, relaxation training (RT) and placebo treatment recommended that considering the cost, side effects and temporary benefits of drug treatment, CBT as a first line therapy for chronic insomnia warrants consideration.

Polysomnography – when to do?

Polysomnography is required in patients with excessive daytime sleepiness, snoring, apnea spells, a body mass index over 35, narcolepsy, sleep walking, periodic limb movement disorders, failure of treatment (104).

INDIAN LITERATURE

In the area of the sleep disorders Indian studies and literature is too embarrassingly scanty, primarily being review articles and replication of western literature (105), few cases reports e.g. fluoxetine induced augmentation of methylphenidate in primary hypersomnia (106).

PRACTICING GUIDELINES FOR INSOMNIA:

Treatment of insomnia should be directed at identifiable causes, or those factors that perpetuate the disorders such as temperament and life style, ineffective coping and defense mechanism, inappropriate use of alcohol or other substances maladaptive sleep wake schedules, and excessive worry about
poor sleep. Clinical management is multidimensional with psychosocial, behavioral, and pharmacological approaches.

**General treatment recommendation**

Clinician treating sleep disorders should attempt to determine the cause of the disorder before initiating treatment. Secondary sleep disorders generally are best managed by treating the underlying disorder. It is equally important to know, beforehand, the normal psychological variations in sleep structure. Some subjects are known to require sleep of less than six hours, while some require more than nine hours. At the extremes of ages, variations are normally seen; the elderly have a gradual reduction in sleep-both qualitatively and quantitatively. However, Kripke et al (2002) [128] found that sleep of more than 8.5 hours or less than 3.5 hours per night had a mortality risk 15 percent higher than those slept an average of 7 hours per night. A detailed sleep history including episodes of awakening can assist in diagnostic clarification and treatment planning. Spouses or family members can often furnish information on behaviors such as snoring or motor activity. Additional factors that need to be evaluated include current stressors, medication or substances use, psychiatric history and environmental factors that may affect sleep.

Following are the recommendations:

**Practice guidelines for the use of polysomnography in the evaluation of insomnia**

- Polysomnography is not routinely indicated for transient or chronic insomnia.
- It is indicated when sleep apnea or myoclonus is suspected, particularly in the older patients.
- It should be considered if diagnosis is uncertain and behavior or drug therapy is ineffective.
- It is indicated for patients with confusional or violent arousals, particularly if the clinical diagnosis is uncertain.
- It should be considered for circadian rhythm disorder if the clinical diagnosis is uncertain.

**Recommendation – Sleep diary**

Among patients with insomnia, a sleep diary for 1–2 weeks should be kept to serve as a baseline assessment of the sleep problem and to monitor the effectiveness of treatment. A sleep diary kept for a period of 2 weeks is helpful for patients who have insomnia (98). The diary includes the patients’ usual bedtime, the total sleep time, the time until onset of sleep, number of awakenings in the night, medications used, quality of sleep rating and daytime consequences of poor sleep. This record, although subjective, reflects the patient’s perception of the amount and quality of sleep he or she is getting (100). This sleep diary would help the physician in determining the severity of the sleep disturbance, the medications being used, the duration of its use and provide a glimpse into the effectiveness of the present treatment regimens.

Insomnia involves daytime consequences such as fatigue, lack of energy, difficulty in concentrating and irritability that cause marked distress or impairment in social, occupational or other important areas of functioning. As such, among patients with insomnia, there should be an assessment of daytime consequences using the scales available locally.

**Therapeutic options for acute insomnia**

**Recommendations**

Among patients with acute insomnia, appropriate action against the inciting cause would often reverse
the condition but short-term pharmacologic therapy together with behavioral intervention should be initiated when the sleep disturbance persists and causes marked daytime impairment. The cause of acute insomnia can often be traced to a particular inciting event. However, even brief episodes of acute insomnia should be treated appropriately when daytime sequelae are severe. It is important to note that untreated acute insomnia might lead to chronic insomnia (99). The recommended pharmacologic and non-pharmacological treatment options are similar for those with chronic insomnia and will be discussed in greater detail in the recommendations that follow.

**Therapeutic options for chronic insomnia**

**General Recommendation**

Among patients with chronic insomnia educational or behavioral intervention combined with pharmacologic agents is more beneficial than either therapy alone. As chronic insomnia is often due to a myriad of factors, a patient may need multiple treatment modalities.

**Recommendation - Non-pharmacological treatment**

The following non-pharmacologic treatment options may be employed for patients with insomnia:

**Behavioral Therapies**

**Sleep Hygiene Education**

It is the basis of preventive strategy for insomnia and is the approach of first choice once a full assessment has eliminated primary psychiatric or medical disorder.

These are general guidelines, it is usually better to help focus one or two of these principles at a time. Long term outcome data is still scarce to support its use.

- Target environmental factors and health practices that may be helpful or detrimental for sleep
- Effects: Found to be beneficial when used in combination with other non-pharmacological insomnia treatments
- Helps to provide interference of insomnia caused by poor hygiene
- Sleep hygiene suggestions
  - Maintain regular hours of bedtime and arising
  - Avoid heavy meals near bedtime
  - Avoid daytime napping
  - Exercise daily, but not later in the evening
  - Minimize caffeine intake and smoking within 8 hr of bedtime
  - Do not look at clock in night
  - Make bedroom comfortable, preferably slightly cool
  - Do not use alcohol while going to sleep
  - Go to bed only when sleepy
  - Minimize light, noise and excessive temperature during sleep
  - Avoid evening stimulation: substituted radio or relaxed reading for television. Practice evening relaxation routines
Relaxation Therapy
- Insomnia patients tend to have high levels of cognitive, physiologic, and/or emotional arousal both day and night
  • Effects: Progressive muscle relaxation to reduce somatic arousal
  • Imagery training, meditation are used to lower presleep cognitive arousal
  • Consistent daily practice is needed over 2-4 weeks to achieve benefit
  • Professional guidance may be necessary for initial training
  • Yoga may be an effective method for relaxation when done properly (e.g. Shavasana)

Sleep Restriction Therapy
- Goal is to decrease the amount of time in bed to increase the percentage of time spent in bed asleep
  • Helpful for patients who have been increasing their time in bed to increase their actual sleep time
  • Effects: Creates mild sleep deprivation which promotes shorter sleep onset and longer time asleep
  • Patients should stay in bed only as long as their average sleep time; but no less than 5 hr*
    Allowable time in bed is increased by 15-20 min as sleep efficiency improves * Time in bed is increased over a period of weeks until optimal sleep duration is achieved. * Usually keep wakeup time the same and adjust bedtime Instructions to be given to the patient are:
    • Stay in bed for the amount of time you think you sleep each night. (Plus 15 min)
    • Get up at the same time each day.
    • Do not nap during the day.
    • When sleep efficiency is 85% (i.e., sleeping for 85% of the time in bed), go to bed 15 min earlier.
    • Repeat this process until you are sleeping for 8 hours or the desired amount of time.
    • Example: If you report sleeping only 5h a night and you normally get up at 6 AM, you are allowed to be in bed from 12:45 AM until 6 AM.

Stimulus Control Therapy
- Based upon the theory that insomnia is conditioned response to temporal (bedtime) and environmental (bedroom/bed) cues that are associated with sleep.
  • The approach is also based on the hypothesis that the sleep environment has become associated with a state of greater arousal specific to presleep factors heard from insomniac patients that they are able to fall asleep in the living room, but not in their bedroom.
  • Effects: Sleep onset and sleep maintenance difficulties can be reduced with stimulus control therapy
    • Bed and bedroom should be associated with rapid onset of sleep
    • Go to bed only when sleepy
    • Use bed only for sleep (or sex)
• Get out of bed and go to another room when unable to fall asleep and return only when sleepy
• Keep regular morning arising regardless of duration of sleep the night before

Cognitive Therapy
• Identify faulty beliefs and attitudes about sleep and replace them with more adaptive ones
• Effects: Has been shown to have positive results on insomnia especially when combined with other techniques
• Goal is to provide reassurance to patients regarding beliefs about sleep
• Eg 'not everyone has 8 hr of sleep', patient may feel refreshed with less, assistance in dealing with bedtime apprehension
• Attempt to decrease the cycle of insomnia, emotional distress, dysfunctional thoughts which can cause further sleep disturbances

Paradoxical Intention
In paradoxical intention, the patients is asked to try not to sleep, which enables the patient recognize the potency of homeostatic sleep regulation. Later it can be suggested to the patient that the body will not allow missing too much sleep.

Cognitive Focusing
This breaks up the ruminating thought process that typically occurs while an insomniac lies awake in bed. In this the patient prepares in advance a series of reassuring thoughts and images on which patients is asked to concentrate, should they wake up during the night.

Thought suppression
Thought stopping and articulatory suppression attempt to interrupt the flow of thought. No attempt is made to deal with thought material as such but rather to alternate thinking. With articulatory suppression the patient is instructed to repeat, sub vocally a word every 3 seconds. Additionally, this technique may be useful during the night to enable rapid return to sleep.

It is important that the therapist encourage the patient to take an active role in the process, rather than passively receiving guidance (Co-scientist model). Active involvement can be encouraged by negotiating an acceptable outcome, which also helps in dispelling unrealistic expectation.

PHARMACOLOGOCAL MANAGEMENT
Recommendation- Pharmacological treatment
Among patients with chronic insomnia, the rational prescription of medications is of utmost importance and should follow these principles:
• start with the lowest effective dose
• use intermittent dosing
• prescribe medications for short-term use
• discontinue the medications gradually
• be alert for rebound insomnia

(246)
Benzodiazepines

- Most commonly prescribed agents for treatment of insomnia
- May be used as adjunctive therapy with behavioral therapy
- Effects: Have been proven effective for short-term insomnia treatment
- Normal sleep patterns are altered
- Use usually limited to a maximum 4 weeks duration
- Long term use increase chances of habituation and withdrawal symptoms
- Tolerance to hypnotic effects develops on repeated administration
- Rebound Insomnia occurs
- Alter sleep patterns least
- Are safer than other drugs in overdose
- Do not significantly induce drug metabolizing enzymes that cause unwanted interactions

Tolerance develops within 3-14 days. Further there are substantial problems of dependence and withdrawal symptoms with long term usage. Hence these should be prescribed rarely and that too for short periods (less than a month) and intermittently (107). Those who are benzodiazepine dependent experience significant rebound insomnia on withdrawal, with vivid dreams and increased REM sleep.

Benzodiazepine-like Hypnotics

Zaleplon

- Effects: Similar hypnotic effects to benzodiazepines but side effects tend to be less
- Does not alter normal sleep patterns and is not associated with tolerance or rebound insomnia

Zolpidem

- Effects: Similar hypnotics effects to benzodiazepines but side effects tend to be less
- Does not alter normal sleep patterns and is usually not associated with rebound insomnia
- Tolerance and dependence has occurred in some patients
- Has been used for up to 6 month usually without withdrawal issues or rebound insomnia upon discontinuation

Zopiclone

- Effects: Decreases sleep latency when compared to placebo and generally increases sleep duration without changing normal sleep patterns
- Rebound insomnia has occurred but not as severe as with benzodiazepines
- Recommended for short-term use limited to maximum 4 weeks duration

Guidelines for Prescribing Hypnotics

- Use the lowest effective dose.
- Use intermittent dosing (alternate night or less)
- Prescribe for short term use (< 4 weeks) in the majority of cases.
- Discontinue slowly
• Be alert for rebound insomnia/withdrawal symptoms
• Advise patients of the interaction with alcohol and other sedating drugs.
• Avoid the use of hypnotics in patients with respiratory disease or severe hepatic impairment and in addiction prone individuals.

Caution with Hypnotics
Hypnotics are relatively contraindicated in patients with sleep disordered breathing, during pregnancy, in substance abuse. Caution should be used in prescribing hypnotics to patients who snore loudly, to patients who have renal, hepatic or pulmonary disease, and to elderly.

Other Agents
Antidepressants
• TCAs have been used in lower doses than used for depression to treat insomnia
• Effects: The sedating antidepressants at usual doses improve insomnia when used in patients with major depression
• Little scientific evidence to support use in non-depressed patients

Antihistamines
• Effects: Generally less effective than benzodiazepines and are associated with daytime drowsiness.

BENZODIAZEPINES LIKE-HYPNOTICS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zaleplon</td>
<td>5-10 mg PO at bedtime</td>
<td>Adverse Reactions</td>
</tr>
<tr>
<td></td>
<td>*Amnesia, anxiety, dizziness, hallucinations, somnolence, impaired coordination, rash, photosensitivity reactions, peripheral edema, GI upset etc</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Special Instructions</td>
<td>*Has been used up to 5 week in trail settings</td>
</tr>
<tr>
<td></td>
<td>5-10 mg PO at bedtime</td>
<td>Adverse Reaction</td>
</tr>
<tr>
<td></td>
<td>*Headache, drowsiness, dizziness, lethargy, abnormal dreams, amnesia, rash, GI upset etc</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Special Instructions</td>
<td>*Has been used for up 6 months usually without withdrawal issues or rebound insomnia upon discontinuation</td>
</tr>
<tr>
<td></td>
<td>7.5-15 mg PO at bedtime</td>
<td>Adverse Reaction</td>
</tr>
<tr>
<td></td>
<td>*Bitter taste, somnolence, dizziness, headache, GI upset, psychiatric and paradoxical reactions, amnesia, rebound insomnia and withdrawal symptoms</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Special Instructions</td>
<td>*Recommended for short term use limited to maximum 4 week duration</td>
</tr>
<tr>
<td>Drug</td>
<td>Dosage</td>
<td>Remarks</td>
</tr>
<tr>
<td>------------------</td>
<td>---------------------------------------------</td>
<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Alprazolam</td>
<td>Half-life: 12-15 hr</td>
<td>Adverse Reactions&lt;br&gt;Dependence and withdrawals symptoms can occur especially in patients with history of drug dependence</td>
</tr>
<tr>
<td>Bromazepam</td>
<td>Half-life: 12-32 hr</td>
<td>Prolonged use of agents with longer half lives may provide next day anxiolytic action and decrease rebound hypertension but they can cause daytime sleepiness cognitive impairment, and in co-ordination</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>0.5mg PO at bedtime</td>
<td>Elderly patients should receive lower doses&lt;br&gt;Short-term use (&lt;4 week) to avoid dependence and withdrawal symptoms</td>
</tr>
<tr>
<td>Dipotassium</td>
<td>Half-life: 19-60 hr</td>
<td></td>
</tr>
<tr>
<td>Clorzapate</td>
<td>5-10 mg PO at bedtime</td>
<td></td>
</tr>
<tr>
<td>Estazolam</td>
<td>1-2 mg PO at bedtime</td>
<td></td>
</tr>
<tr>
<td>Flunitrazepam</td>
<td>0.5-2mg PO at bedtime</td>
<td></td>
</tr>
<tr>
<td>Flurazepam</td>
<td>15-30mg PO at bedtime</td>
<td></td>
</tr>
<tr>
<td>Lorazepam</td>
<td>1-4 mg PO at bedtime</td>
<td></td>
</tr>
<tr>
<td>Lormetazepam</td>
<td>1-2 mg PO at bedtime</td>
<td></td>
</tr>
<tr>
<td>Midazolam</td>
<td>Half-life: 6-8 h, active metabolite:48-96 hr</td>
<td></td>
</tr>
<tr>
<td>Nitrazepam</td>
<td>5-10 mg PO at bedtime</td>
<td></td>
</tr>
<tr>
<td>Oxazepam</td>
<td>Half-life: 2-7 hr</td>
<td></td>
</tr>
<tr>
<td>Temazepam</td>
<td>20 mg PO at bedtime</td>
<td></td>
</tr>
<tr>
<td>Triazolam</td>
<td>Half-life: 1.5-5 hr</td>
<td></td>
</tr>
<tr>
<td>Lormetazepam</td>
<td>1-2 mg PO at bedtime</td>
<td>Adverse Reaction&lt;br&gt;Dependence and withdrawals symptoms can occur esp in patients with history of drug dependence</td>
</tr>
<tr>
<td>Midazolam</td>
<td>7.5-15 mg PO at bedtime</td>
<td>CNS effects (eg sedation, drowsiness, muscle weakness, ataxia. Less commonly slurred speech, vertigo, headache, confusion). Symptoms decrease after continued use</td>
</tr>
<tr>
<td>Nitrazepam</td>
<td>Half-life: 24-30 hr</td>
<td>Prolonged use of agents with longer half lives may provide next day anxiolytic action and decrease rebound hypertension but they can cause daytime sleepiness cognitive impairment, and in co-ordination</td>
</tr>
<tr>
<td>Oxazepam</td>
<td>15-30 mg PO at bedtime</td>
<td>Triazolam: Has been withdrawn from the market in several countries because of reports of confusion, amnesia and unusual behavior</td>
</tr>
<tr>
<td>Temazepam</td>
<td>20 mg PO at bedtime</td>
<td>Special Instruction&lt;br&gt;Elderly patients should receive lower doses&lt;br&gt;Short-term use (&lt;4 week) to avoid dependence and withdrawal symptoms</td>
</tr>
<tr>
<td>Triazolam</td>
<td>Half-life: 1.5-5 hr</td>
<td></td>
</tr>
</tbody>
</table>
MANAGEMENT OF OTHER SLEEP DISORDERS

Treatment of Primary Hypersomnias

Clinical management is controversial owing to the lack of controlled studies. Most widely used, and successful of the treatment options available are the stimulant compounds. For patients intolerant of, or insensitive to stimulants, stimulating antidepressants, MAOI or SSRI classes may be used. Methysergide may be effective in resistant cases; however, cautions regarding pleural and retroperitoneal fibrosis should be taken.

Treatment of Narcolepsy

Major goals of treatment of narcolepsy include:

a. To improve quality of life.
b. To reduce excessive daytime sleepiness (EDS)
c. To prevent cataplectic attacks

The major wake promoting medications are:

Modafinil - Preferred due to efficacy, safety, availability, and low risk of abuse and diversion (110). Modafinil is FDA approved for EDS treatment. Usual dosing is 200-400 mg each morning.

Amphetamine and Dextroamphetamine (10 mg morning)

Methamphetamine (10-20 mg bd)

Pemoline - carries the rare risk of fatal hepatic toxicity

Pharmacological treatment of cataplexy, sleep paraoxysm, and hypnagogic hallucination include administration of activating SSRI such as fluoxetine (10-20 mg/d) and TCA such as protriptyline (10-40 mg/d) and clomipramine (25-50 mg/d)

Sodium oxybate Xyrem, appears to be well tolerated and beneficial for treatment of cataplexy, EDS and inadvertent sleep attacks (108,109)

Practice guidelines for the use of stimulants in the treatment of narcolepsy:

- A polysomnogram and the Multiple Sleep Latency Test should establish the diagnosis of narcolepsy.
- Stimulants should be used to alleviate daytime sleepiness, not to maximize performance.
- Pemoline, methylphenidate, dextroamphetamine, methamphetamine, and modafinil have proven efficacy.
- The recommended maximum daily dose for some of the stimulants used to treat narcolepsy are as follows:
  • Pemoline 150 mg
  • Methylphenidate 100 mg
  • Dextroamphetamine 100 mg
  • Methamphetamine 80 mg
- Combining short and long-acting stimulants may be indicated in some patients.
- Tolerance is most likely to occur in treatment with high-dose amphetamines.

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- Most female patients should discontinue taking stimulants during pregnancy. Caution is urged in prescribing stimulants to nursing mothers. Adequate nocturnal sleep and planned daytime naps (when possible) are important preventive measures (111).

Treatment of sleep apnea
It may be alleviated by weight loss, avoidance of sedatives, use of tongue retaining devices, breathing under positive pressure through a mask - CPAP (continuous positive airway pressure), sleep position training (112,113)

TCAs are sometimes used in sleep apnea in young adults (not in older people).

The newer shorter acting non-benzodiazepine hypnotics seem to be safer in these patients and may be considered in those who snore.

Surgery, including pharyngoplasty; may relieve heavy snoring (114)

To date, nasal CPAP remains the initial treatment of choice for moderate to severe sleep apnea; however discontinuation of nasal CPAP even for one night results in complete reversal of the gain made in daytime alertness (116)

Treatment of Circadian Rhythm Sleep Disorder- Delayed and Advanced Sleep phase disorder
Primary disorder should be identified and treated. Clinical management includes chronobiological strategies to shift the phase position of the endogenous oscillator in the appropriate direction. e.g. exposure to bright light in the morning advances the delayed sleep phase i.e. individuals will become sleepy earlier in evening (115) On the other hand administration of bright light in evening acts to delay circadian rhythm, thus individuals will get sleep later in the evening. Light is usually administered in dose of 2500 lux for 2 hours per day, although the ideal intensity and duration are yet to be determined. For some individuals, spending more time outdoors in bright sunlight may be sufficient to treat the sleep phase disorders.

Treatment of Shift Work
No totally satisfactory method currently exists for managing shift work problems. Appropriate exposure to bright lights and darkness may push the circadian pacemaker in the correct direction and help stabilize its phase position, especially in association with the use of dark glasses outside and blackout curtains at home to maintain darkness at the appropriate times for promotion of sleep and shifting of the circadian pacemaker (117). Naps may also be useful in reducing sleep loss. Modest amounts of coffee may maintain alertness early in the shift but should be avoided near the end of the shift.

Treatment with melatonin has been found to be less successful than timed bright light exposure in aiding adjustment to shift work.

Treatment of Jet Lag
Some efforts before departure may be useful to prevent or ameliorate these problems. For people who plan to readjust their circadian clock to the new location, it may be possible to move the sleep-wake and light-dark schedules appropriately before departure. Good sleep hygiene principles should be respected before, during, and after the trip. Whereas adequate fluid intake on the plane is necessary to avoid dehydration, alcohol consumption should be avoided or minimized because it causes diuresis and may disrupt sleep maintenance.
On arriving at the destination, it may be preferable to try to maintain a schedule coinciding with actual home time if the trip is going to be short. Unfortunately, the exact protocols have not been established in all instances yet and require further research and experimentation.

In addition to synchronizing the clock with the new environment, sleep and rest should be promoted by good sleep hygiene principles, by avoidance of excessive caffeine and alcohol, and, possibly, by administration of short duration hypnotics. Care should be taken, however, to avoid hangover effects or amnesia associated with hypnotics. Because individual responses to sleeping pills vary considerably from person to person, it is often helpful to develop experience with specific compounds and doses before departure.

**Transient Situational Insomnia**

This develops after a change in sleeping environment or after a significant life event. Recovery is usually rapid (within a few weeks). Treatment is symptomatic, with intermittent use of hypnotics and resolution of the underlying stress.

**Insomnia associated with other medical disorder**

Treatment of the underlying medical disorder or symptom is the most useful approach.

**Substance Induced Sleep Disorder**

An important aspect in evaluation of sleep disorders is to review the use of medications and other substances including prescription, over the counter and recreational drugs, as well as alcohol, stimulants, narcotics, coffee and nicotine and exposures to toxins, heavy metals etc.

In general, treatment should be aimed at the primary diagnosis after management of any acute withdrawal condition that may exist. Non-pharmacological treatment approaches include sleep hygiene and sleep restriction, attention to general nutrition, physical health and psychosocial support. Use of benzodiazepines or other hypnotics is not generally recommended because of cross tolerance or deliberate or inadvertent overdose. Karam Hage and Brower et al 2000 (118) reported that the sleep of abstinent alcoholic patients improved when treated with gabapentin.

SSRIs are associated with over arousal and insomnia in some patients, but commonly with sedation in other (119). Co-administration of bedtime trazodone in a double-blind, placebo-controlled study was effective in managing fluoxetine induced insomnia in depressed patients (120).

**General Approaches to the Clinical Management of Sleep Disorder in Psychiatric Patients**

Nonspecific treatment, such as use of sleep hygiene principles, is often helpful for the both the sleep complaints and the underlying psychiatric disorder.

In general, avoid polypharmacy. Sleeping pills should be prescribed reluctantly to patients who receive adequate doses of antidepressants. Although co-administration of a benzodiazepine may improve sleep during the first week of antidepressants therapy, a low dose of zolpidem, zaleplon, trazodone, or other sedating antidepressants at night in addition to the antidepressants may be less likely to produce tolerance and may have additive antidepressant benefits. Antipsychotic medications should
PARASOMNIAS: MANAGEMENT

Sleep Walking

After establishing the diagnosis advice must be given regarding making the room and surrounding area safe. It may even be necessary for the patient to sleep on ground floor. Family reassurance is necessary.

Attention to family and psychological uses- reduction in overall tension in house hold- may reduce sleepwalking. Anxiety reduction techniques may be helpful.

Some patients respond to administration of benzodiazepines (BZDs) or sedating antidepressants at bedtime (4). Schenk et al (1986) (4) reported that the long term use of BZD in adults with injurious parasomnia, was safe and effective.

Treatment of Sleep Terror Disorder

Nocturnal administration of BZDs has been reported to be beneficial by suppressing delta sleep.

REM Sleep Behavior Disorder

Clonazepam 0.5-1mg, bedtime, is usually remarkably successful in controlling the symptoms. Patients and family should be educated about nature of the disorder and warned against about injuring themselves or others. Carbamazepine has also been found to be useful (122). Treatment with the acetylcholinesterase inhibitor Donepezil has also been found to be effective (121).

Nightmares

The disorder is usually self limited in children but can be helped sometimes with psychotherapy, desensitization or rehearsal instruction (127). Secondary nightmares, as in PTSD, can be difficult in treat. They are some times brought out by REM-suppressing drugs, in which case, the treatment is to gradually discontinue the medication, if possible.

Periodic Limb Movement in Sleep (PLMS)

Because the pathogenesis of PLMS is not usually known, treatment is often symptomatic. Dopaminergic agents such as L-Dopa (25-100mg/d), Pergolide (0.05-1mg), Pramipexole (0.25-0.875mg), generally provide the most effective treatment for PLMS and restless leg syndrome (123-126). Clorazepam, opiates like oxycodone and propoxyphene, anticonvulsants like carbamezepine and gabapentin (124), have also been found to be effective.

Pharmacologic Treatment Options In RLS/PLMS
Practice guidelines for the treatment of nocturnal myoclonus (NM) and restless legs syndrome (RLS)

The diagnosis of nocturnal myoclonus or restless legs syndrome should be established by the patient’s history, bed partner report, and possible polysomnogram.

Secondary causes of NM and RLS should be evaluated and treated.

Levodopa/carbidopa, oxycodone, propoxyphene, carbamazepine, and clonazepam have proven efficacy. Gabapentin and clonidine have possible efficacy.

Close physician monitoring of adverse effects is required.

Iron supplementation is useful for RLS patients with iron deficiency.

Most female patients should discontinue taking medication during pregnancy.

No information is known about the use of medication in children with NM or RLS.

Scope of this document:

The guidelines are aimed to ensure uniform standards of care. The psychiatrists should consider, but not restrict to the recommendations made, as these are neither comprehensive nor definitive. They are also meant principally for adults patients. Owing to poverty of work in this area in India, these guidelines must be regarded only as a preliminary effort, requiring further modification and revisions. Hence, feedback and suggestions from all mental health professionals will be more than welcome.
An algorithm for the differential diagnosis of persistent sleep disorder complaints

Step 1: Consider the role of general medical conditions, substance use, and other mental disorders

- Yes → A: Sleep disorder due to a general medical disorder
- No

Step 2: If the individual suffers from the sleep involved in shift work, frequently crosses over time zones, or has abnormal timing of sleep

- Yes → A: Circadian rhythms sleep disorder
- No

Step 3: Are the symptoms predominantly events during sleep (i.e., abrupt awakening, frightening dreams, walking about while sleeping)

- Yes → A: Nightmare disorder
- No

Step 4: If the primary complaint is insomnia (i.e., difficulty initiating or maintaining sleep)

- Yes → A: Primary Insomnia (if symptoms persist for more than 1 month)
- No

Step 5: If the primary complaint is excessive sleepiness or hypersomnia

- Yes → A: Narcolepsy (sleep attacks)
- No

Step 6: If clinically significant criteria are not met for a previously described specific disorder, or if one wants to note symptoms as a more complete evaluation is being conducted

- Yes → Dyssomnia not otherwise specified

A: Sleep disorder due to a general medical disorder
B: Breathing-related sleep disorder
C: Substance-induced sleep disorder
D: Other mental disorder and/or insomnia related to a mental disorder

A: Circadian rhythms sleep disorder
B: Sleep-awake schedule disorder
C: Delayed sleep phase
D: Advanced sleep phase
E: Shift work
G: Non-24-h day

A: Nightmare disorder
B: Sleep terror disorder
C: Sleepwalking disorder
D: Periodic limb movements or restless legs syndrome
E: Nocturnal panic attacks

A: Primary Insomnia (if symptoms persist for more than 1 month)
B: Dyssomnia not otherwise specified (symptoms persist for less than 1 month)

A: Narcolepsy (sleep attacks)
B: Primary hypersomnia (prolonged sleep episodes, regular daytime sleep episodes)
C: Dyssomnia not otherwise specified
D: Breathing-related sleep disorder (see step 1A)
E: Kleine-Levin syndrome
F: Menstrual cycle-associated hypersomnia
G: Atypical or winter depression

Dyssomnia not otherwise specified
Diagnostic approach to insomnia

Sleep History
Include:
- Hours of sleeping
- Sleep and awakening times
- Sleep Position
- Type of bed, pillows, etc
- Eating habits in evening
- Alcohol intake

Discuss sleep patterns with bed partner

Any chronic medical conditions?

Arthritis, allergies, congestive heart failure, and benign prostatic hypertrophy can all affect sleep patterns.

Medication?
Decongestants, beta agonists, corticosteroids, beta blockers, diuretics, antidepressants, and H2 blockers commonly disturb sleep.

Any family history of sleep dysfunction?

Any psychiatric illness?
Anxiety, depression, and panic disorder can disrupt sleep patterns

Any symptoms of daytime sleepiness, excessive snoring, apnea, or BMI>35

If Yes
Referral for Polysomnography

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Treatment Algorithm of Insomnia

Diagnosis of insomnia ➔ Identify and treat the associated conditions

Pharmacological treatment ➔ Non-pharmacological treatment

- Non-prescription medications
- Prescription medications

- Non-prescription medications

Antidepressants
- 1. Amitriptyline
- 2. Trazodone
- 3. Nortriptyline

Non-benzodiazepine Hypnotics
- 1. Zolpidem
- 2. Zaleplon

Benzodiazepines (BZDs)
- Short acting
  - 1. Triazolam
- Intermediate acting
  - 1. Temazepam
  - 2. Estazolam
- Long-acting
  - 1. Flurazepam

1. Stimulus control
2. Paradoxical Intention
3. Muscle relaxation
4. Sleep restriction
5. Temporal control
6. Improving sleep hygiene
References


51. Lader M. Anxiety or depression during withdrawal of hypnotics treatments. J Psychosom Res 1994;38:113-123.


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