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Insomnia and Mild Cognitive Impairment

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Insomnia and Mild Cognitive Impairment

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Abstract

Insomnia is a common problem in older people, especially in patients with mild cognitive impairment (MCI) whose circadian rhythm is often compromised. Insomnia exerts such a toll on caregivers that it is frequently the primary reason for seeking to institutionalize their loved ones. Three different types of insomnia are recognized: sleep-onset or initial insomnia, sleep maintenance or middle insomnia, and early morning awakening or late insomnia. Nocturnal hypoglycemia, as a cause of middle insomnia, is the main focus of this case study. Other types of insomnia are also briefly reviewed. The management of insomnia is then discussed including sleep hygiene, the usefulness and potential drawbacks of dietary supplements, nonprescription over-the-counter preparations and prescription hypnotics. Sleep architecture is then briefly reviewed, emphasizing the importance of its integrity and the role of each sleep stage.

Keywords

Alzheimer's/dementia, caregiving and management, cognition, confusional states, anxiety

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Objectives

At the end of this case, presentation readers will:

1. Recognize common causes of insomnia in older patients with mild cognitive impairment, with special emphasis on nocturnal hypoglycemia as a cause of sleep maintenance insomnia or middle insomnia.
2. Appreciate the nonpharmacological management of insomnia.
3. Know potential benefits and drawbacks of sleep aids available over-the-counter.
4. Appreciate the usefulness, limitations, and adverse effects of commonly used hypnotics.
5. Understand the importance of sleep architecture and the main functions of each sleep stage.

Case Presentation

Characters

- Esther, 72 years old, has mild cognitive impairment, diagnosed about 2 years ago. She also has diabetes mellitus, well-controlled by oral hypoglycemics. She has been living with her daughter, son-in-law, and granddaughter, since her husband died about a year ago, because she was unable to take care of the large house she lived in. Her daughter and son-in-law converted the den into a room for her. Esther is physically independent, drives her own car and is socially active. Apart from the hypoglycemics, she is on no other medication. Her hearing is impaired; she wears hearing aids.
- Miranda is Esther's daughter.
- Donald is Miranda's husband.
- Mary Lee is Miranda and Donald's 4-year-old daughter.

Scenario

It is close to 6:00 p.m. The family is sitting at the dining room table. Esther is not hungry and does not eat. Miranda asks her if she is going to eat. Esther replies she is not really hungry, she's been sitting all day reading

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and plans to exercise for at least an hour on the stationary bike before going to bed. She explains that she borrowed a 90-min documentary DVD on climate change from the library and plans to watch it while exercising. Donald asks her if she would like some of the cheesecake he bought. Esther again declines, excuses herself and goes to exercise on the stationary bicycle.

After exercising for over an hour, Esther returns to the front room where Miranda and Donald are watching a TV movie. Mary Lee is sleeping in her own room. Esther says that she plans to shower and then will head straight for bed. She enjoyed her exercise session and now feels physically tired but mentally relaxed and ready for a good night sleep. "Isn't it too early for bed?" Donald asks. "It's only about eight in the evening." Esther replies, "No, I'm ready for bed."

Donald asks, "Aren't you going to eat anything before going to bed? What about the cheesecake I just bought?" Esther replies, "No thanks. I'm so tired I'll fall asleep as soon as my head hits the pillow." Donald persists, "Shall I prepare you a cup of herbal tea or hot chocolate or how about some cookies?" Esther replies, "No thanks. I'll just shower and then go to straight to bed." Almost in unison Miranda and Donald say, "OK, have a good night's sleep."

Miranda is somewhat concerned: "Do you think she is depressed? She hardly touched her food and had nothing to eat since we had that cup of tea when you came back from work." Donald is not concerned. He only hopes she has a good night's sleep because he has a very heavy day at work the following day and plans to leave home at about 5:00 a.m. He says,

> My main concern is that we have a repeat of last week when she woke up at about 2:00 a.m., could not fall asleep and tried to prepare breakfast. In the process she made so much noise that she even woke up the neighbors.

On the way to their bedroom they notice that lights are out in Esther's room. "Keep your fingers crossed." Donald murmurs in Miranda's ear as they head toward their bedroom.

It is about 2:00 a.m. Everybody is sound asleep except for Esther. She's been awake for about 30 min. She goes to the bathroom again, then returns to bed. She cannot sleep. She tosses and turns and is wide-awake. She tries to read but gives up. She looks for her hearing aids but drops them on the floor and cannot reach them because they rolled under her bed. She switches on the TV but cannot hear so she increases the volume so high that it wakes up Miranda and Donald. Very quickly, an altercation develops between Miranda and Donald. Tempers flare. Now Mary Lee is awake and crying. Donald states that the time has come for Esther to be placed in a nursing home or assisted living facility because he needs a full night sleep: "This cannot continue! Your mother is jeopardizing my career and destroying our marriage."

Case Analysis

Turning Points/Triggers That Lead to This Aberrant Behavior Include

No food/drink for a few hours before going to bed. Esther did not have dinner and it is questionable how much she ate earlier that day. Therefore, by 2:00 a.m. her blood glucose levels would have been sufficiently low to stimulate the sympathetic nervous system and release of catecholamines (adrenaline and noradrenaline) which would then wake her up and induce anxiety and irritability (Borbely, Mattmann, Loepfe, Strauch, & Lehmann, 1985). The catecholamine surge also may induce cardiac arrhythmias, which may reduce the stroke volume, cardiac output, and subsequently cerebral blood flow and perfusion thus worsening the patient's cognitive deficit. Nocturnal hypoglycemia is likely to occur in Assisted Living Facilities and nursing homes when the last substantial meal of the day can be served as early as 5:00 p.m. Even though snacks are usually available later in the evening and night, residents may not eat them, because they often do not feel hungry or have difficulties reaching the dining area.

Esther also has diabetes mellitus and is on oral hypoglycemics. As such, she is much more likely to develop bouts of hypoglycemia. The impact of hypoglycemia is significant in terms of sleep quality and next-day function (Brod, Wolden, Christensen, & Bushnell, 2013; Evans et al., 2013; Harris et al., 2014), even among the younger population with diabetes mellitus (Brod, Christensen, & Bushnell, 2012; Fulcher et al., 2014; Iscoe & Riddell, 2011; Jennum et al., 2015; Khunti et al., 2016; Klimontov & Myakina, 2017; Munshi et al., 2011; Porcellati, Lin, Lucidi, Bolli, & Fanelli, 2017; Speight et al., 2016; Yang, Kim, Baek, Kim, & Park, 2016).

Could it have been avoided? Esther should have been encouraged to eat dinner regardless of whether she was feeling hungry. This would have ensured that her plasma glucose level does not drop to the extent of stimulating the sympathetic nervous system. Similarly, after exercising, she should have had a healthy snack: for example, a glass of milk, chocolate, or hot herbal tea with honey and a few cookies. This would provide the patient with enough glucose and complex carbohydrates to prevent the plasma glucose level from dropping during the night.

Sugary drinks contain sucrose which breaks down into glucose, but their effect on plasma glucose levels is short-lived. The effect of complex carbohydrates on the blood glucose level is much longer lasting because they first have to be digested and then absorbed through the intestines. Hence, a good combination is a hot sugary drink and complex carbohydrate, such as a couple of cookies or a slice of whole grain bread. The sugary drinks will have an almost immediate effect on plasma glucose level that may last a few hours, especially if consumed hot as this may enhance absorption through

the gastro-intestinal tract. Ice cream is another option. Efforts therefore should have been made to emphasize that in Esther's case the purpose of eating is to ensure a good night's sleep and should be taken "for medicinal purposes" regardless of whether or not Esther feels hungry.

Hypoglycemia could be confirmed by assaying the blood glucose level. The very early nocturnal awakening and ensuing episode could have easily been avoided had Esther eaten or had a hot sugary drink with a few cookies or some of the cheesecake her son-in-law bought earlier that day. As a similar episode happened earlier that week, it should not have been too difficult to convince Esther of the need to eat and drink before going to bed. It also would have been very useful to measure her blood glucose level and share the results with her physician to ensure she is getting the right medication, in the right dose for her diabetes. Patients treated for diabetes are more likely to develop hypoglycemia.

Physical exertion and showering before going to bed. During physical exertion, the liver and muscles break down their glycogen stores to produce glucose which is needed to meet the energy needs of the exercising muscles. When exercise stops, the liver and muscles extract glucose from the blood stream to replenish their glycogen stores (Oda & Shirakawa, 2014). This may occur over a period of a few hours and may lead to hypoglycemia.

Strenuous exercise increases body temperature which also may interrupt sleep. Esther exercised for over an hour and then proceeded to shower before going to bed. Depending upon the temperature of the water and duration of the shower her body temperature could have been kept elevated. Having Esther exercise earlier in the day may also increase her appetite and desire to eat dinner.

Could it have been avoided? This episode could have been avoided had Esther exercised and showered earlier in the day.

Esther sleeps in a windowless room:A converted den. There are no windows in Esther's room, as such, she is not getting any visual cues about the time of the day or night to adjust her circadian rhythm. When she wakes up, she has no idea what time it is and whether or not she should stay in bed and be quiet while her daughter, son-in-law and granddaughter are still sleepy.

Could it have been avoided? A large well-lit, visible wall clock or the time projected on the wall immediately across her bed would have reminded Esther of the time of the day, would have helped her readjust her circadian rhythm, and would have encouraged her either to stay in bed or to be quiet so as not to wake up the rest of the household.

Esther dropped her hearing aids and could not retrieve them. This prevented Esther from hearing the TV and as a result she had to increase the volume to such an extent that it woke up the rest of the household.

Could it have been avoided? Given that hearing is such an important element of communication with other people and that hearing aids are so important to a person sharing accommodation with others, they should be easily accessible, even in the dark, especially if the person lives in a windowless room, as is the case with Esther. Hearing aids or headphones should be kept in an illuminated easily accessible container or tray. Similarly, sound from the TV could be channeled straight to the patient's ears through earplugs or headphones. These are easier to use than hearing aids which need to be inserted through the external auditory meatus: a particularly difficult task in a person who has just woken up and may have apraxia as part of the underlying neurocognitive disorder. A small night light bulb with red wavelengths could be utilized for visibility without hindering sleep (Brainard et al., 2015; Schmerler, 2015).

Esther turned on the TV. As Esther did not have her hearing aids, she was unable to hear the TV without increasing the volume to such an extent that it woke up Miranda and Donald then subsequently Mary Lee.

Could it have been avoided? The TV could have been connected electronically to her hearing aids or headphones. This would have allowed her to increase the volume as high as needed without anyone else being even aware that the TV is switched on.

If possible, it may have been better to have Esther's room in a more remote part of the house where any noise generated by Esther would not be easily transmitted to the other bedrooms. Sound proofing would be another option, albeit an expensive one.

Still another option would have been not to have a TV in Esther's bedroom, especially as the light rays emitted from the TV may interfere with the release of melatonin from the pineal body in the brain and this per se, may interfere with the circadian rhythm.

Stress, depression, and insomnia. Stress and Depression oftentimes follows the death of a loved one and major life changes. Given that within the past year, Esther not only lost her husband but also moved out of her home into her daughter's home, Esther could have been experiencing undiagnosed stress and/or depression. Depression interferes with sleep: patients tend to wake up early in the morning and have a difficult time falling back to sleep. Early morning awakening is indeed one of the common manifestations of depression. The stress of these major life changes could have increased Esther's cortisol level, which also contributes to insomnia (Botts, 2010; Dumbell, Matveeva, & Oster, 2016; Spencer, Chun, Hartsock, & Woodruff, 2017).

Could it have been avoided? It is important to ascertain whether Esther is depressed. Screening for depression is

recommended in all older patients, especially those with mild cognitive impairment. The successful management of depression is often associated with an improvement of cognitive functions. A number of screening questionnaires are available.

It is also important to detect suicidal ideation, as the potential for suicide is high in older people, especially men, particularly those who live on their own. In Esther's case, it is therefore relevant to evaluate her for depression and suicidal ideation. Depression and suicidal ideation in patients with impaired cognitive functions are discussed in subsequent case studies.

Case Discussion: Scope of the Problem

Chronic insomnia is defined as difficulties falling asleep or remaining asleep occurring 3 or more times a week for 1 or more month (Winkleman, 2015; *Diagnostic and Statistical Manual of Mental Disorders* [5th ed.; *DSM-5*]; American Psychiatric Association, 2013). It affects about one third of the adult population (Winkleman, 2015). About 50% of patients with chronic insomnia have underlying psychiatric diseases including depression, suicidal ideation, anxiety, impaired cognitive functions, and dementia (Winkleman, 2015). Sleep complaints are associated with an increased mortality of common diseases such as ischemic heart diseases, cerebro-vascular accidents and neoplastic lesions (Gooneratne et al., 2006). Not diagnosing or misdiagnosing the cause of insomnia may have serious nefarious outcomes such as when sleep apnea is missed and the patient prescribed a hypnotic or a sedative (Trevorrow, 2010). The incidence of insomnia is higher in older than younger adults and is associated with poor health and cognitive impairment (Ancoli-Israel, 2009; Arbus & Cochen, 2010).

Diagnostic Criteria of Insomnia (DSM-5)

Insomnia is defined as a dissatisfaction with the quantity or quality of sleep due to difficulties initiating sleep (sleep-onset or initial insomnia), maintaining sleep (sleep maintenance or middle insomnia), or early morning awakening with inability to return to sleep (late insomnia), occurring at least 3 times a week for at least 1 month, despite adequate opportunities to sleep and provided it is not due to another medical or mental disease, the effects of medication or substance abuse, including alcohol and is not due to another sleep-wake disorder (*DSM-5*). Patients with nonrestorative sleep complain of a poor sleep quality and of not feeling rested or refreshed on waking up: They still feel tired.

Apart from nighttime sleep difficulties, insomnia is often associated with worsening cognitive impairment, especially difficulties with attention, concentration, memory, and performance of simple daily tasks. Patients are also often irritable, anxious, depressed, and may exhibit mood lability.

Causes of Insomnia

The causes of insomnia can be classified into three groups: extrinsic causes, intrinsic causes, and those related to the individual's lifestyle.

Extrinsic causes of insomnia include change of bed/bedroom, uncomfortable bed, noise, excessive lighting, too low or too high an environmental temperature, and excessive humidity or dryness. A number of medications also may induce insomnia including selective serotonin reuptake inhibitors, theophylline, thyroid hormone, diuretics, beta-blockers, antiarrhythmics, clonidine, sympathomimetic stimulants, corticosteroids, and medications containing caffeine. Over-the-counter medications also may predispose to insomnia including nicotine replacement, energy boosters, and other preparations containing alcohol or caffeine.

Intrinsic causes include a number of diseases which may interfere with the quantity and quality of sleep including restless leg syndrome, sleep apnea, gastro-esophageal reflux disorders (giving rise to heartburn), chronic obstructive airways disease (dyspnea), nocturnal asthma (dyspnea), congestive heart failure (dyspnea, orthopnea, paroxysmal nocturnal dyspnea, nocturnal polyuria), coronary artery disease (chest pain), arrhythmias (palpitations), diabetes mellitus (polyuria, peripheral neuropathies, peripheral vascular disease), inflammatory conditions (pain), arthropathies (pain), respiratory tract infections (cough, dyspnea), urinary tract infections (dysuria and frequency), any infection (pain), renal calculi (pain), and neoplasia (pain). Obesity also predisposes to insomnia. A number of psychiatric disorders also may induce insomnia.

Several lifestyle habits also may induce insomnia including having naps throughout the day, consuming heavy meals or undertaking strenuous physical exercises shortly before going to bed, excessive alcohol or caffeine intake before going to bed and mental stress. Other habits that may detrimentally affect the quantity/quality of sleep include watching TV, using a laptop computer, or other electronic devices shortly before going to bed, or while in bed. These may interfere with melatonin production and the circadian rhythm. If it is necessary to use these technologies before bedtime, it is recommended to use the night shift capabilities which will diminish the blue light and display the more yellow–orange end of the spectrum (Gronli et al., 2016).

In many instances it is not one factor, but rather a combination of factors that lead to insomnia: Each factor on its own may not be sufficient to induce insomnia, but the combination of factors leads to insomnia. It is therefore important to identify these factors and address them while managing insomnia. As much as possible hypnotics should be prescribed only after identifying

and addressing the cause(s) of the insomnia (Arbus & Cochen, 2010).

Assessing the Severity and Impact of Insomnia

Given that assessment of sleep quality and quantity is such a subjective individual issue, a number of questionnaires are available to objectively assess sleep quality and quantity (Trevorrow, 2010). A good sleep history from the patient and bedroom partner, if available, is the first step in assessing the type and severity of the insomnia taking into account the various extrinsic factors that may lead to insomnia. Enquiries should also be made about the patient's lifestyle habits that may affect sleep. A thorough clinical examination is then recommended to identify the cause(s) of the insomnia. Depending on the findings, a few laboratory tests and imaging studies may be required.

A number of procedures can be used to assess sleep quality and quantity including electroencephalograms (EEGs), polysomnography, audio and video recordings, measurement of various physiological parameters such as pulse rate, respiratory rate, eye movement, arousal thresholds, and a number of other parameters. Sleep laboratories are also widely available, although it should be pointed out that only a small number of patients will require such studies.

A number of smartphone apps, devices, and gadgets are becoming available to track sleep pattern and offer targeted advice that may help achieve a better sleep pattern. Some of these devices also provide cranial stimulation. Unfortunately, the background research on most of these is limited and their long-term efficacy and safety are not known.

Management of Insomnia

Although managing insomnia, all three groups of factors (extrinsic, intrinsic, and lifestyle habits) need to be addressed to tailor the management strategy to the individual circumstances of the particular patient and maximize the impact of the management strategy. Although managing insomnia nonpharmacological means should be tried before prescribing hypnotics. Regardless of the cause(s) of insomnia, good sleep hygiene promotes restorative, good quality, and good quantity sleep.

A number of nonpharmacologic measures are available to manage insomnia. Their success largely depends on the cooperation of the patient, her motivation and willingness to pursue these lines of management. Sleep specialists trained in behavioral medicine may be able to help patients with insomnia replace lifestyle habits responsible for their insomnia with good habits that enhance the quality and quantity of sleep and its restorative functions. The goal of relaxation techniques is to train the patient to relax and free herself of mental impediments to sleep.

The main goal of sleep restriction to manage insomnia is to increase the patient's sleep drive by reducing the time in bed (but no less than 5 hr per 24 hr) and inducing a sleep debt. The patient is expected to respond by sleeping better during the hours she is allowed to sleep, thus normalizing her circadian rhythm (Phillips, Klerman, & Butler, 2017). Once the patient responds favorably, the amount of time spent in bed is gradually increased.

The main goal of cognitive behavioral therapy (CBT) is to restructure the patient's dysfunctional behaviors and/or beliefs that perpetuate insomnia. As a result, sleep latency is shortened, frequency and duration of nocturnal awakenings are reduced and total sleep time is lengthened (Cervena et al., 2004). The main limitations of CBT include the number of sessions required to achieve good results, the relatively small number of therapists available and the low patient adherence. Web-based CBT is available and may be helpful.

Sleep Hygiene: Measures to Improve Quality and Quantity of Sleep

Sleep quality and quantity may be improved by going to bed at about the same time every day, including weekends. If the individual cannot sleep within 20 to 30 min, she should not stay in bed. She should get out of bed, get engaged in some relaxing activity and then return to bed when she feels tired. Watching TV may be counterproductive, especially if watched in bed and if the program watched is violent, scary, or needs the individual to concentrate on the show such as watching mystery movies. Ideally, the material watched should be light-hearted and relaxing.

Physical exercise is recommended, but not within 2 hr of bedtime. Vigorous physical exercise is associated with an increased production of catecholamines and stimulation of the sympathetic nervous system which interfere with sleep. A hot sweet drink, preferably with honey and accompanied by one or two cookies, about 30 min before going to bed will ensure the blood glucose levels do not drop while the patient is asleep. A warm bath before going to bed will help relax the patient.

The bedroom should be dark or dimly lit, not noisy and be at a comfortable temperature and degree of humidity. The mattress should be firm, the bedsheets clean with no wrinkles and no foreign bodies such as breadcrumbs, food particles, or other material. Pillows should be comfortable.

Sleep Hygiene: Measures to Avoid to Improve Quality and Quantity of Sleep

Mentally demanding, irritating activities should be avoided for at least an hour before going to bed. The following should be avoided within 2 hr of going to bed: naps, vigorous physical exercise, tobacco use, heavy meals

especially spicy food which may induce heartburn, alcoholic drinks, high fluid intake (the induced polyuria may interfere with sleep quality and quantity), and caffeine containing drinks and food, such as dark chocolate.

Nonprescription, Over-the-Counter, Pharmacologic Management of Insomnia

The primary active ingredient of most nonprescription sleeping tablets is an antihistamine compound such as diphenhydramine or doxylamine. Antihistaminics are also acetylcholine antagonists. Per se they are not hypnotics, but, given their sedating effect, they induce drowsiness and thus help the person initiate and maintain sleep. Short-term adverse effects include dizziness, impaired coordination, nausea, headaches, constipation, dysuria, urinary retention, palpitations, tachycardia, thickened bronchial secretions, diaphoresis, and blurred vision. Their administration also may induce cognitive impairment and toxic psychosis, especially in older people. They also may induce unsteadiness and increase the risk of falls. This can be quite problematic in older patients with dementia especially as the half-life of these medications tends to be prolonged in older people. Alcohol intake also potentiates their effect. Although these medications have been available for a very long time, their long-term safety is not known.

Dietary Supplements

Dietary supplements do not come under the regulation of the Food and Drug Administration (FDA). As such, therefore, they are rigorously tested for neither safety nor effectiveness. Similarly, their quality and label accuracy are not verified by the FDA. Furthermore, although touted as "natural" some may contain other active biologic ingredients that may not be mentioned on the package or label, but nevertheless may interact with other medications. It is therefore relevant to enquire about any "dietary supplement" the patient may be taking on a regular basis and identify any possible interaction with the patient's other medications.

Valerian and chamomile are readily available and often touted as sleeping aids. Valerian root extract, however, contains more than 100 specifically identified substances (Harvard Medical School Special Health Report, 2013). Our understanding of the mode of action of these compounds is still limited.

Melatonin

Melatonin facilitates sleep initiation and improves sleep quality without altering sleep architecture (Zhdanova, 2005). The effects of melatonin are mediated through specific melatonin receptors. The response to melatonin in older people, however, is often reduced because of the often age-related reduced functional potency of melatonin receptors (Zhdanova, 2005).

Melatonin is available over the counter and often used to induce sleep. A review of the available literature by the Agency for Health care Research and Quality concluded that melatonin reduced sleep latency to a greater extent in people with delayed sleep phase syndrome, suggesting that it exerts its effects by resetting the circadian rhythm rather than acting as a hypnotic (Buscemi et al., 2004). Melatonin also may be effective at alleviating the effect of symptoms of jet lag (Vosko, Coldwell, & Avidan, 2010). The administration of exogenous melatonin is safe in the short term (Buscemi et al., 2004).

Melatonin is synthesized from tryptophan in the pineal body, located behind the third ventricle in the brain. Approximately 90% of melatonin is cleared in a single passage through the liver. A small proportion is excreted unchanged in the urine. Long-term effects and safety of melatonin are not known.

Hypnotics

A number of hypnotics are available to induce sleep. Although they should be used in the lowest dose and for the shortest period, to maintain their efficacy and limit the adverse effects, many patients are on hypnotics for long periods of time. Four main classes of hypnotics are available: benzodiazepines, nonbenzodiazepines, antidepressants and melatonin receptor agonist.

Benzodiazepines act by enhancing the activity of the neurotransmitter Gamma Aminobutyric Acid (GABA). The profile of various benzodiazepines is dependent on their half-lives and how quickly and for how long their action lasts. Their main drawback is that they alter sleep architecture (Borbely et al., 1985; Wagner & Wagner, 2000). The sleep they induce is therefore not as restorative as natural sleep. Their main adverse effects include psychomotor and memory impairment, next-day impaired mental alertness, sedation, drowsiness, and unsteadiness that may increase the risk of falls. Other side effects include exacerbation of depression and suicidal ideation, aggressive behavior, amnesia, and hallucinations. Many patients develop tolerance and need higher doses. Abruptly stopping their administration often leads to rebound insomnia with an increased risk of restlessness, irritability, and rarely convulsions. Benzodiazepines are best suited for the short-term treatment of insomnia. Available benzodiazepines have a wide range of half-lives: triazolam (1.5 to 5.5 hr), temazepam (8.8 hr), alprazolam (12 to 16 hr), lorazepam (14 hr), estazolam (10 to 24 hr), clonazepam (20 to 50 hr), diazepam (30 to 50 hr), and flurazepam (40 to 100 hr).

Nonbenzodiazepines are at least as effective as benzodiazepines at inducing sleep and improving subjective sleep quality (Uchimura et al., 2006). Their main advantages include their relatively short half-life and that they

induce less psychomotor and memory impairment than benzodiazepines and antidepressants (Schneider, 2002). They, nevertheless alter the sleep architecture, especially in older patients, albeit to a lesser extent than benzodiazepines (Chinoy, Frey, Kaslovsky, Meyer, & Wright, 2014). Their main adverse effects include nausea, headaches, drowsiness, dizziness, repeated falls, nightmares, disorientation, agitation, and somnambulism, including nocturnal eating, walking, and even driving. Dependence, rebound insomnia and withdrawal symptoms occur less frequently than with benzodiazepines (Wagner & Wagner, 2000). Available nonbenzodiazepines used for insomnia have shorter half-life: Zaleplon (1 hr), zolpidem (2.5 to 3.1 hr), and eszopiclone (6 hr). Extended release preparations are available but are associated with changes in sleep architecture and impaired physical performance during nighttime awakening and the following day and therefore may impact nefariously on the patient's safety (Kleykamp, Griffiths, McCann, Smith, & Mintzer, 2012).

A number of antidepressants are also used for the management of patients with insomnia, including the following: Selective Serotonin Reuptake Inhibitors (citalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline), Serotonin and Norepinephrine Reuptake Inhibitor (venlafaxine), Serotonin modulator (trazodone), tetracyclic (mirtazapine), and tricyclics (amitryptiline, doxepin, nortryptiline, and trimipramine). Main adverse effects include dry mouth, dizziness, daytime, and drowsiness. Ramelton is a melatonin receptor agonist. Its main adverse effect is that it may exacerbate depression.

Sleep Structure/Architecture and Cycles

Nocturnal sleep occurs in cycles. It has two distinct components: Quiet sleep and Rapid Eye Movement (REM) sleep. Dreams occur during the latter component. Quiet sleep is also known as non-REM sleep and has three stages.

The first stage: "Quiet or non-REM sleep" represents the transition between wakefulness to light sleep. During this stage, the eyes close and the brain, deprived of visual input, slows down. At the beginning of this stage, brain waves on the EEG are in the "alpha-wave pattern," a rhythmic pattern of about 10 cycles per second. As Stage 1 progresses brain waves on the EEG slow down to 4 to 7 per second: "theta wave pattern." Thinking slows down as well as the heart rate, breathing rate, and most physiological activities. Body temperature starts to fall. Muscles relax but movement may still occur and the person may change positions looking for a most comfortable position. Eyes move slowly. The person gradually loses spatial orientation, but is easily jarred awake. Stage 1 of non-REM sleep is often referred to as "an idling brain in a movable body" and usually lasts about 5 min.

During the second stage of non-REM sleep the eyes are closed, not moving, the heart rate and respiratory rate slow down further, EEG exhibits large slow waves intermingling with bursts of activity known as sleep spindles. Body temperature decreases. The brain disconnects itself from outside sensory input and begins the process of memory consolidation. On the EEG K-complexes are evident: They represent a sort of vigilance system that, if necessary, allows the person to wake up. Stage 2 lasts 10 to 25 min. If the person is not woken up, she proceeds to Stage 3.

During the third stage, also known as deep sleep, large slow waves: "delta waves" become prominent on the EEG. This stage is also sometimes referred to as the "Slow Wave Sleep." The blood pressure drops, breathing and heart rates slow down further to about one third below the level during wakefulness. The brain is less responsive to external stimuli and it is difficult to wake up the person sleeping in this stage. During this stage, the pituitary gland releases growth hormone which stimulates tissue growth and allows the body to renew and repair itself. The immune system is also stimulated. This stage lasts about 30 min in young adults, but gets progressively shorter as individuals age. When subjects are deprived of this stage, they wake up feeling less refreshed and when offered the opportunity of sleeping again, tend to rapidly descend to the third stage, thus spending more time in this stage and less time in Stages 1 and 2.

REM sleep is characterized by dreaming and has been described as an "active brain in a paralyzed body": the eyes, while closed, move rapidly, body temperature rises, blood pressure increases, heart, and breathing rates increase. The sympathetic nervous system is activated and launches the fight-or-flight response, but the body is essentially paralyzed except for occasional twitches and the REMs. During this stage, the brain processes information received during the day. REM-sleep facilitates learning and enhances memory. The initial REM-sleep stage lasts only a few minutes, but as the night progresses this stage tends to become longer. In a way, the body having physically repaired and renewed itself during the third stage, now addresses the person's mental and cognitive functions. When persons who have been deprived of REM sleep are allowed to sleep uninterrupted, they rapidly go to the REM-sleep stage. This is referred to as "REM rebound."

Non-REM sleep alternates with REM sleep, each cycle lasts 60 to 90 min. On average people go through three to five cycles a night. As the night progresses, the time spent in REM and Stage 1 sleep gets longer, while Stage 3 gets shorter and may be altogether absent.

As individuals grow older, sleep latency, which is the time needed to transition from wakefulness to Stage 1 non-REM sleep tends to be prolonged, while the total duration of nocturnal sleep tends to decreases. Similarly, time spent in Stage 2 increases while the time spent in

Stage 3 and REM-sleep decreases. Sleep is also more fragmented and daytime naps are more frequent than in younger adults (Arbus & Cochen, 2010).

Summary/Teaching Points

- Nocturnal hypoglycemia is a cause of sleep disturbances: middle or late insomnia and is often precipitated by lack of food or physical exertion before going to bed.
- Causes of insomnia can be classified into three groups due to extrinsic factors, intrinsic factors, and lifestyle habits. All three groups should be addressed as often the etiology of insomnia, especially in older patients with dementia is multifactorial.
- Sleep hygiene plays an important role in maximizing the quality and quantity of sleep. Patients and caregivers should be made aware of the various measures to undertake and those that need to be avoided. Sleep hygiene should be prescribed to patients with insomnia, in conjunctions with other measures taken.
- A number of dietary supplements and sleep aids are available. They are not regulated by the FDA. There is a paucity of good research on their use to facilitate and maintain sleep.
- A number of nonprescription medications are available. The active ingredient in most is an antihistamine compound such as diphenhydramine. They are not hypnotics, but induce drowsiness which may lead to unsteadiness and falls. They tend to have long half-lives and therefore physical and mental performance the following day(s) may be impaired, particularly in older patients.
- Melatonin is available over-the-counter in the United States. It is secreted by the pineal body and helps maintain the circadian rhythm. It facilitates sleep initiation and improves sleep quality without altering sleep architecture.
- Prescription hypnotics include benzodiazepines, nonbenzodiazepine, antidepressants and a melatonin receptor agonist. The former three alter sleep architecture to various degrees and therefore may interfere with the quality of the sleep they induce.
- Strategies to reduce the impact of watching TV on other cohabitants include using a headset connected directly or electronically to the TV, using a room as far away as possible from other bedrooms and sound proofing the TV room.
- Circadian rhythm disorders can be helped by a large wall clock visible from a distance, a 24-hr clock, exposure to bright lights early afternoon to reset the melatonin diurnal rhythm and administration of melatonin in late evening.

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