REVIEW ARTICLE

Diagnosis and treatment of sleep disorders: a brief review

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ABSTRACT

Sleep is a function of all living organisms; it is essential for survival and maintaining mental and physical health. There are five stages of sleep in humans. The disturbance of the sleeping pattern or behaviors refers to sleep disorders. There are several sleep disorders; the most common disorders include insomnia, sleep apnea, and narcolepsy. The present study aims to review previous literature available and provide insight on the diagnosis and treatment of the most common sleep disorders. The online databases Google Scholar and PubMed as well as Research Gate were used to perform a literature search for publications published between 2013 and 2019, without any date or language restrictions. We used a combination of relevant search terms "sleep disorders, treatment, diagnosis, management." We obtained 33 articles related to our subject; after the revision of the titles of the articles, the abstract, reviewing the main titles inside articles and the years of publications, we included only 10 articles. We excluded 23 articles as they were either duplicate of other articles, repeating the same information, or not concentrating on the current subject. The correct diagnosis of sleep disorder was found to be a crucial step for the correct and successful management. The treatment of the patient is based on the type of disease, its severity, and the comorbidities of the patient.

Keywords: Sleep disorders, classification, diagnosis, treatment.

Introduction

Sleep is a function of living organisms; it comprises one-third of human life [1]. Sleep is essential for survival, and it plays an important role in maintaining mental and physical health [2]. Sleep requirements vary between individuals and different ages; however, the general average requirement for healthy adults ranges from 7 to 8 hours of sleeping per night [3]. The normal sleep of humans can be categorized into two types; non-rapid eye movement sleep and rapid eye movement sleep [2]. The human continues to cycle through the previous types every 90 minutes [2]. Regarding the stages of sleep, there are five stages; stage one is the superficial sleep and it lasts for 5-10 minutes only. This first stage is a transition from the awake state to going to sleep state. This stage is characterized by loss of muscle and slows down movement. The second stage is light sleep, it lasts for 20 minutes, and it accounts for 50% of sleep in adults. This stage is characterized by the stop of eye movement, reduction of muscle movement, slow heart rate, and drop in body temperature may occur. The third stage is the beginning of slow wave deep sleep. The fourth stage lasts for 30 minutes, and it is also deep sleep, and it is the restorative period of sleep. The last and fifth stage is the rapid eye movement phase, and it occurs rapidly

after the fourth stage, and it accounts for 25% of sleep in adults. This stage is characterized by increased activity of the brain and the occurrence of dreams. This stage also involves an increase of respiration, heart rate, and occurrence of atonia resulting in temporary paralysis [4]. Insufficient or poor sleeping is associated with a variety of dysfunction in most of the systems of the body, including neurological disorders, endocrine, metabolic, and higher cortical function [1]. Sleep disorders are defined as conditions that are characterized by a disturbance of the usual pattern or behaviors of the sleeping. These disorders cause impairment in day functions and distress [5]. Sleeping disorders can appear as complaints of abnormal movements during sleep, insufficient sleep, or an excessive amount of perceived sleep [1]. Almost 40

million individuals in the United States are affected by chronic sleep disorders and wakefulness [6]. The most prevalent sleep disorders include sleep apnea, insomnia, narcolepsy, and restless legs syndrome [6]. Sleep disorders cause 38,000 cardiovascular deaths annually [7]. Sleep disorders had an impact on the driving, social activities, and work of the individuals [6]. This review was done to highlight the classification, diagnosis, and treatment of the most common sleep disorders.

Literature Search

Searching for the scientific articles to be included in this review was performed using online searching through scientific websites. We searched for articles related to the current subject through scientific websites such as Google Scholar and PubMed as well as Research Gate using several keywords, including "sleep disorders, treatment, diagnosis, management." We obtained 33 articles related to our subject; after the revision of the titles of the articles, the abstract, reviewing the main titles inside articles and the years of publications, we included only 10 articles. We excluded 23 articles as they were either duplicate of other articles, repeating the same information, or not concentrating on the current subject. The included articles were published between 2013 and 2019. The current review was written under specific titles.

Discussion

Diagnosis of sleep disorders

Diagnostic classification of sleep disorders

There are here diagnostic classification systems to classify sleep disorders used by clinicians [2]. These classifications include the Sleep Disorders section of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) [8], the International Classification of Diseases, Tenth Edition (ICD-10) [9], and the International Classification of Sleep Disorders, Third Edition (ICSD-3) [10]. The DSM-5 classification is used by general medical and mental health clinicians who have no experience in sleep medicine. This system has a great concordance with the ICSD-3 compared to other previous editions. This classification system does not divide the adult and pediatric diagnosis; it involves 10 disorder groups and they include insomnia, narcolepsy, hypersomnolence, breathing-related sleep disorders, Non-rapid eye movement sleep (NREM) sleep arousal disorders, rapid eye movements (REM) sleep behavior disorder, restless legs syndrome, nightmare disorder, circadian rhythm sleep awake disorders, and substance/medication-induced sleep disorders [2].

The ICD-10 is a classification system for the classification of sleep conditions. It is far less complex compared to the ICSD-3 classification. This classification categorizes the sleep disorders into organic and non-organic origin; the organic sleep diseases focus on the medically and neurologically based disorders as well as the disease of the nervous system such as narcolepsy and sleep apnea,

whereas the non-organic sleep disorders classification involves behavioral and mental disorders, and they are further classified into three types of conditions; parasomnias, dyssomnia, and sleep disorders secondary to psychiatric and medical disorders [2].

The ICSD-3 is the most advanced classification system of sleep disorders, and sleep experts use it. This classification involves six main clinical categories; each category includes further sections, as shown in Table 1 [2]. The ICSD-3 provides general diagnostic criteria for each disorder [2].

History and physical examination

A detailed and accurate history taken from the patient combined with a sleep questionnaire can provide critical information for the diagnosis. Most sleep complaints fall into three groups; excessive sleepiness, insomnia, or abnormal behavior during sleep [6]. The examiner should investigate the main complaint by asking when the symptoms begin, the pattern since onset and the associated factors that may participate or predisposed to the illness, and improved or worsened symptoms [11]. The second step in the physical examination is to assess the impact of the sleep complaint on the life of patients and asking about the schedule of meal and sleep, the sensation of the restless leg, snoring, sleep hygiene, gasping, coughing, sweating, bruxism, periodic limb movement, mouth dryness, abnormal behaviors during sleep, excessive movements during sleep, sleep paralysis, daytime sleepiness, hallucinations, and presence of cataplexy. Caffeine, nicotine, illicit drugs, and alcohol intake should be investigated. Reviewing the patent psychiatric, medical, and surgical history, as well as previous treatments, should be investigated. Also, a family history of sleep disorders should be determined. The working diagnosis can be outlined based on the chief complaint, information of the questionnaire, the patient's history, and sleep diary [6].

Laboratory investigations

Laboratory investigations are performed to assess sleep disorders and then treat them. The laboratory tests used include multiple sleep latency test (MSLT), actigraphy, video-polysomnogram (PSG), nocturnal penile tumescence monitoring (NPT), electroencephalography (EEG), including 24-hours ambulatory EEG, the PSG, and maintenance of wakefulness test (MWT) [6]. The MSLT is used for assessing the complaints of moderate to severe sleepiness in patients with mild to moderate obstructive sleep apnea syndrome (OSAS), the confirmation of the diagnosis of narcolepsy, unknown causes of excessive sleepiness, idiopathic hypersomnia, some circadian rhythm disorders [12,13]. NPT is an adjacent diagnosis of impotence that assesses sleep-related erections. EEG is performed for patients with suspected epilepsy [6]. PSG is a nocturnal complete laboratory-based monitoring which records several variables during sleep. It includes electrooculogram, EEG that assess sleep staging, submental electromyogram,

Table 1. ICSD-3 diagnostic classification and sections.

Classification	Disorders
Insomnia	-Chronic insomnia
	-Short-term insomnia disorder
	-other insomnia disorder
Sleep-related breathing disorders	-Obstructive sleep apnea (Adult, pediatric)
	-Central sleep apnea syndromes (with Chenyne-stroke breathing, due to a medical disorder without Chenyne-stroke breathing, due to high altitude periodic breathing)
	- Central sleep apnea results from a medication or substance (central sleep apnea, of infancy, of prematurity, treatment central sleep apnea)
	-Sleep-related hypoventilation disorders (congenital central alveolar hypoventilation syndrome, obesity hypoventilation syndrome, late-onset central hypoventilation with hypothalamic dysfunction, sleep-related hypoventilation caused by a medication or substance, idiopathic central alveolar hypoventilation, sleep-related hypoventilation due to a medical disorder, sleep-related hypoxemia disorder)
Central disorders of hypersomnolence	- Narcolepsy type 1
	- Narcolepsy type 2
	- Idiopathic hypersomnia
	- Kleine-Levin syndrome
	- Hypersomnia due to a medical disorder
	- Hypersomnia due to a medication or substance
	- Hypersomnia associated with a psychiatric disorder
	- Insufficient sleep syndrome
Circadian rhythm sleep-wake disorders	- Delayed sleep-wake phase disorder
	- Advanced sleep-wake phase disorder
	- Irregular sleep-wake rhythm disorder
	- Non-24-hours sleep-wake rhythm disorder
	- Shift work disorder
	- Jet lag disorder
	- Circadian sleep-wake disorder not otherwise specified
Parasomnias	-NREM-related parasomnias (sleep-related eating disorder, confusional arousals, sleepwalking, sleep terrors)
	-REM-related parasomnias (REM sleep behavior disorder, nightmare disorder, recurrent isolated sleep paralysis)
	- Other parasomnias (exploding head syndrome, sleep-related hallucinations, sleep enuresis, parasomnia due to a medical disorder, parasomnia due to a medication or substance, unspecified parasomnia)
Sleep-related movement disorders	- Restless legs syndrome
	- Periodic limb movement disorder
	- Sleep-related leg cramps
	- Sleep-related bruxism
	- Sleep-related rhythmic movement disorder
	- Benign sleep myoclonus of infancy
	- Propriospinal myoclonus at sleep onset
	- Sleep-related movement disorder due to a medical disorder
	- Sleep-related movement disorder due to a medication or substance
	- Sleep-related movement disorder, unspecified
Other sleep disorders	–

respiratory effort, oximetry, electrocardiogram, oral or nasal airflow, position monitoring, and anterior tibialis electromyogram. Modified Posterior Spinal Fusion (PSF) includes split-night studies, daytime nap PSG, and portable recording studies [6].

The MWT is less commonly used compared to MSLT; it is performed mainly to assess improved alertness following therapeutic interventions [12-14].

The major sleep disorders and their treatments

Insomnia

Insomnia indicates nightly complaints of insufficient sleep or feeling restless after the habitual sleep episode [6]. Almost more than one-third of adults suffer transient insomnia at some point in their lives [10]. Women are more affected by insomnia, with a prevalence range of 10%-30%

[15,16]. In about 40% of cases, insomnia can develop into persistent and more chronic conditions. Insomnia diagnosis occurs when the patient reports sleep dissatisfaction and daytime symptoms such as mood disturbance, impaired attention, and sleepiness for at least three nights per week and a duration of more than 3 months [10]. The diagnosis and treatment of subtypes of insomnia are similar to that of insomnia [1]. The treatment of insomnia includes non-pharmacological and pharmacological therapies. The treatment strategy should consider the presence of comorbidities that may lead to sleep disturbance, such as periodic limb movement in sleep. Reduction of insomnia symptoms can be performed through initial counseling and education about the practice of good sleep. Cognitive-behavioral therapy is helpful for persistent insomnia; it may have equal or even better influence than pharmacological treatment; its impact is also longer lasting [17-21].

Pharmacological therapy is helpful in the treatment of insomnia in case of stress setting and as adjuvant therapy with behavioral treatment. Several factors should be considered when selecting the medications, and they include the predominant type of compliant, the frequency of insomnia symptoms, the duration of treatment, age of the patient, and comorbidities [1].

The medications used frequently in the treatment of insomnia include benzodiazepines, hypnotics (zolpidem complete remission (CR), zolpidem, zaleplon, intermezzo, and eszopiclone), melatonin antagonists, antidepressants, orexin antagonists, and antihistamines. Benzodiazepines have the characteristics of being cheap and ubiquitous; however, they are associated with several problems such as high frequency of falls, hypotension, excessive sedation, muscle relaxant effect, cognitive effect, losing efficacy after a long duration of usage. The hypnotics have the advantages of short-acting (Zaleplon, Intermezzo), approved by the Food and Drug Administration (FDA) for chronic insomnia. However, they have several side effects such as oversedation; some have potential lose efficacy, and parasomnia [1,6].

Sleep-related breathing disorders

The primary sleep disorder is sleep apnea, which is characterized by pauses of breathing during sleep. There are three main types of sleep apnea, and they are obstructive, central, and complex sleep apnea. The former type refers to the cessation of airflow for at least 10 seconds, and it results from the collapse of the upper airway during sleep. Whereas the central sleep apnea refers to the interruption of airflow when there is a lack of effort to breath, and it usually arises from the brain respiratory centers to the muscles that control the breathing process. The complex type is a combination of both previous types [1]. Moderate to severe sleep apnea is prevalent among 30%-50% of males and 11%-23% of females in the general middle-aged population [22,23]. The clinical symptoms of sleep apnea include choking, gasping, loud snoring, excessive sleeping, morning headache, and fatigue [24]. The diagnosis of such disorder can be performed through polysomnography to quantify sleep apnea by the number of respiratory events that occur per hour of sleep. Five events per hour are required for the diagnosis of sleep apnea with clinical symptoms (Apnea-Hypopnea Index ≥5) [25]. Mild sleep apnea scores between 5 and 14, whereas moderate case scores between 15 and 29, and severe sleep apnea scores more than 30. Several screening scales have been developed to identify the patients at risk, such as the STOP-BANG questionnaire [26]. The treatment of sleep apnea varies according to the severity of the case. Conservative therapy, such as avoiding supine position and weight loss, is helpful for mild cases. Mild to moderate cases can get benefits from an oral appliance such as mandibular advancement devices of obstructive sleep apnea. Surgical intervention includes the soft palate, nasal, and maxillomandibular surgeries; these interventions do not cure sleep apnea, but they help sleep apnea severity [1].

Central disorders of hypersomnolence

This category of disorders includes narcolepsy and hypersomnia. Narcolepsy is a disease that refers to the rapid eye movement sleep regulation. Central hypersomnia is caused by narcolepsy type one and two, idiopathic hypersomnia, and recurrent hypersomnia [10]. The classic symptoms include sleep paralysis, hypnagogic hallucinations, and sleepiness. The diagnosis can be performed clinically, and for confirmation of sleepiness, a MSLT is required [1]. The treatment of sleepiness begins with armodafinil or modafinil. If these therapies are not effective or tolerated, stimulants such as amphetamine/dextroamphetamine or methylphenidate can be used. These medications can worsen arrhythmias and blood pressure. These drugs have not been approved for usage during pregnancy [1].

Circadian rhythm sleep-wake disorders

In normal situations, the sleep phase of the circadian rhythm occurs about 2 hours after melatonin secretion onset. It may occur earlier or later than society-driven scheduled sleep time, leading to advanced or delayed sleep-awake phase disorder [1]. Delayed sleep-wake phase disorder is common among young adults, and adolescents and its prevalence is 16% and 7%, respectively. It also accounts for 10% of patients with chronic insomnia [10]. The diagnosis and treatment of the patient require an accurate assessment of the circadian phase of the patient. The circadian rhythm sleep-wake disorder is misdiagnosed as insomnia or hypersomnia [1]. The treatment of circadian rhythm sleep-wake disorder is based on melatonin (1 hour before required bedtime in delayed phase disease) and timed bright or blue light (morning for delayed phase disorder, and afternoon for advanced phase disorder) [27]. Tasimelteon is helpful for the non-24 hours sleep-wake phase disorder [28].

Parasomnias

The most common non-rapid eye movement parasomnias include night terrors, confusional arousals, and somnambulism. Parasomnias are characterized

by a wide variety of behaviors [1]. The most common medication used for the treatment of rapid eye movement is clonazepam [29]. Clonazepam should be used with caution among dementia patients; it also may result in excessive sedation. Melatonin is another option that is safer and inexpensive [30]. Melatonin is of the same efficacy as clonazepam for decreasing the frequency of dream-enactment episodes [31].

Sleep-related movement disorders

This category includes restless legs syndrome, which is the most common sleep-related movement disorder; its prevalence ranges from 10% to 15% among patients with age ranges of 27-41 years old [32]. It is characterized by uncomfortable crawling or creeping sensation inside the calves and pains in the legs associated with a desire to move the legs, which is partially relieved by physical activity [1,6]. This syndrome can be idiopathic or secondary to iron deficiency [6]. The clinical history can make the diagnosis of the patient [1]. Treatment of restless legs syndrome can start with dopamine agonists, gabapentin enacarbil, or gabapentin. Also, other agents are effective such as ropinirole, cabergoline, levodopa, pramipexole, and pergolide. In advanced cases, opiates can be considered. In idiopathic restless legs syndrome, pneumatic compression devices and intravenous ferric carboxymaltose can be effective [33]. There are several medications associated with exacerbation of restless legs syndrome, including sedating antihistamines, some antidepressants, and antipsychotics [34,35].

Conclusion

The correct diagnosis of sleep disorder is a critical step for the management of the disease. The diagnosis of sleep disorders depending on the history taking and physical examination combined with laboratory investigations if required, then the classification and correct diagnosis are made. Once the diagnosis is performed, the physician can prescribe medication based on the disorder the patient complains about, the severity of the disease, and comorbidities of the patient.

List of Abbreviations

DSM-5	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
EEG	Electroencephalography
ICD 10	International Classification of Diseases, Tenth Edition
ICD 3	International Classification of Diseases, Third Edition
MSLT	Multiple sleep latency test
MWT	maintenance of wakefulness test
NPT	Nocturnal penile tumescence monitoring
PSG	Polysomnogram

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