Sleep disorders in clinical practice

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Abstract

Sleep is essential for life in humans and is important to maintain homeostasis. As sleep comprises almost 1/3 of our life, sleep disorders should be systematically examined, and sleep disturbances must be carefully treated to avoid systematic complications. Although sleep disorders are common in clinical practice, they are frequently undiagnosed. The most common sleep disorder is insomnia, nevertheless Obstructive Sleep Apnea (OSA) represents a growing clinical entity with acceptable morbidity and mortality in clinical practice nowadays. Non-respiratory sleep disorders are also important to be recognized and properly treated, especially insomnia, as they can cause health-related quality of life impairment, if left untreated. In addition, circadian rhythm sleep-wake disorder is an emerging sleep disorder entity, distinct from other neurological conditions, with which clinicians should be familiar in order to provide effective interventions. Sleep disorders should be carefully identified and addressed and targeted treatment must be provided by sleep medicine specialists in properly equipped facilities.

Key words: *sleep medicine; sleep apnea; CPAP; circadian rhythm; shift work*

INTRODUCTION

Although the field of medicine is recent, there are historical, literary and scientific descriptions that have contributed to current knowledge. Sleep disorders have been recognized and described since Hippocrates's age, who wrote, "I have known many persons in sleep groaning and crying out, some in a state of suffocation, some jumping up and fleeing out of doors, and deprived of their reason until they awaken", obviously depicting manifestations of sleep disorders.

But many years have passed in the history of medicine and the systematic study of sleep has led to the conception that sleep is a dynamic process involving complex neural activation. Brain activity is different during wakefulness and sleep and this can be recorded by the means of electroencephalography (EEG). Sleep is an on-off phenomenon and there are no intermediate states between wakefulness and sleep. The study of EEG is important in sleep medicine and it can demonstrate distinct stages and patterns; thus, sleep can be divided in rapid-eye movement sleep (REM) and non-REM.

Sleep is essential for human life and is important to maintain homeostasis. While the function of sleep remains unknown, studies have identified relationships between sleep and anatomical, physiological, or psychological traits [1]. As sleep comprises almost 1/3 of our life, sleep disorders should be systematically examined, and sleep disturbances must be carefully treated to avoid systematic complications [2].

SLEEP DISORDERED BREATHING

Sleep disordered breathing is a term used to describe several respiratory disturbances that occur during sleep. The International Classification of Sleep disorders (ICSD-3) classifies sleep disordered breathing into the following

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categories: obstructive sleep apnoea syndrome (OSA), central sleep apnoea syndrome (CSA) and sleep-related alveolar hypoventilation.

The underlying pathophysiology is different in these sleep disturbances. Regarding OSA, which is the most common sleep disorder in clinical practice, the upper airway obstruction is usually caused by abnormal anatomy (e.g. fat accumulation) and/or abnormal control of the muscles that maintain the patency of the upper airway. In CSA, a dysfunction of the ventilatory control is attributed to the dysfunction of respective central neurons, resulting in loss of ventilatory effort and control.

OSA

Obstructive sleep apnoea (OSA) is highly prevalent and its management represents an increasing part of clinical respiratory practice in developed countries. OSA is supposed to be one of the most common chronic respiratory disorders in adults together with asthma and Chronic Obstructive Pulmonary Disease (COPD). The increasing awareness of the public and medical community about the relationships between snoring, excessive daytime sleepiness, cardiovascular disease, diabetes and OSA has resulted in large numbers of patients referred to outpatient sleep clinics [3].

A landmark study in 1996 that attempted to estimate OSA prevalence in the general middle-aged population showed that obstructive sleep apnea syndrome (OSAS) affected 4% of males and 2% of females [4]. But the prevalence is increasing due to the recent obesity epidemic and can be as high as 25% in the sub-population of middle-aged men [5]. Approximately 80% of OSA patients are obese and obesity is a recognized risk factor for OSA. Body weight changes can affect the severity of the syndrome. It is known that a 10% weight gain predicts an approximate 32% increase in apnea hypopnea index (AHI), whereas a 10% weight loss predicts a 26% decrease in AHI. Several papers have shown a higher prevalence of OSAS in the elderly. The age distribution of patients first diagnosed with OSAS generally peaks at age 50 yrs. Epidemiological studies have shown that OSA is much more prevalent in males and the phenotype is easily recognized as it is usually characterized by obesity and the symptoms of snoring, witnessed apnoeas and daytime sleepiness. Females with OSA may have blunt symptoms of mood alteration or morning headaches [6].

OSA symptoms can be divided into symptoms recognized during sleep by the bed partner (night-time symptoms) and symptoms experienced by patients themselves during the day after the sleep (daytime symptoms). Snoring with periods of pause of breathing and choking can make the diagnosis straightforward, if witnessed and reported by the bed partner. Typically, these symptoms become worse in the supine position and after alcohol consumption or after a tiring day (Table 1) [7].

There are useful clinical scores that can be used in the screening of patients eligible for attending a dedicated sleep clinic. The most widely used are the Berlin Questionnaire and the STOP-BANG Questionnaire, which can detect OSA symptoms with an acceptable sensitivity up to 87% (Table 2) [8][9].

OSA causes arterial hypertension and is a cardiovascular risk factor; a high apnoea burden can cause cerebrovascular disease, with stroke being the most obvious. Moreover, OSA is an independent risk factor for developing insulin resistance and diabetes. The subsequent daytime sleepiness is a recognized cause of car accidents and fatalities especially when large vehicles are involved [10][11].

CSA

CSA is characterized by recurrent cessations of airflow and simultaneous reduction of the breathing effort. In contrast to OSA, ventilatory impulses generated by the brain stem are lacking in CSA. It is estimated that 10% of breathing disturbances during sleep are of central origin, especially in the elderly. A subtype of CSA is the Cheyne-Stokes respiration pattern, which is characterized by a periodic shift of overshooting and undershooting of the ventilation (crescendo-decrescendo pattern) [12]. The most relevant risk factors for central breathing

Table 1. *Daytime and night-time symptoms in OSA.*

Daytime symptoms	Night-time symptoms
Excessive daytime sleepiness	Snoring
Fatigue	Witnessed apnoeas
Morning dry mouth	Disturbed unrefreshing sleep
Morning headache	Enuresis
Difficulty concentrating	Nocturnal sweating
Irritability	Gastro-oesophageal reflux
Mood changes	
Impaired memory	

Table 2. *The Berlin and the STOP-BANG Questionnaires for detecting OSA symptoms.*

Berlin Questionnaire	STOP-BANG Questionnaire
Has your weight changed?	Do you snore loudly?
Do you snore?	Do you often feel tired, fatigued, or sleepy during daytime?
Snoring loudness.	Has anyone observed you stop breathing or choking/gasping during your sleep?
Snoring frequency.	
How often have your breathing pauses been noticed?	Do you have or are being treated for high blood pressure?
	Body Mass Index more than 35 kg/m2?
Are you tired during wake time?	Age older than 50?
Have you ever fallen asleep while driving?	Neck size?
Do you have high blood pressure?	Male gender?
	High risk of OSA: positive answer to ≥3 items
	Low risk of OSA: positive answer to <3 items

disturbances during sleep are cardiovascular diseases, such as atrial fibrillation, heart failure and stroke and chronic renal disease [13].

Obesity hypoventilation syndrome

Obesity hypoventilation syndrome is characterized by elevated PaCO2 (>45 mmHg) during sleep or disproportionately increased PaCO2 relative to levels during wakefulness. There is accompanying arterial oxygen desaturation during sleep and there must be an increased BMI (>30 kg/m^2). This ventilatory derangement is associated with excessive daytime sleepiness, tiredness, morning headaches and poor sleep quality as a result of frequent interruption of sleep with repetitive arousals and CO2 retention [14].

DIAGNOSIS OF SLEEP-DISORDERED BREATHING

The gold standard for diagnosis of sleep disorders and subsequently sleep-disordered breathing is overnight polysomnography. The polysomnogram is a summary output of electrophysiological signals integrating sleep signals, respiratory signals, cardiovascular signals and movement. The recording of sleep states requires acquisition of three main measures: the electroencephalogram (EEG), the electrooculogram (EOG) and the electromyogram (EMG). Respiration is monitored by oronasal flow as well as respiratory effort, movement and snoring. The effects of respiration are also monitored using oximetry and sometimes carbon dioxide monitoring, usually transcutaneous. After having stored all these traces overnight, the analysis of sleep stages together with the cardiorespiratory parameters facilitate the diagnosis of sleep disorders [15]. The high prevalence of OSA in the general population has prompted the scientific community to develop portable home sleep apnoea testing. Indeed, the American Academy of Sleep Medicine advocates the usage of portable sleep apnea testing and monitoring at home. The indications for home apnoea sleep testing approved by the American Academy of Sleep Medicine are: a) in patients with high pretest probability of OSA without comorbidities, b) when sleep-laboratory polysomnography is not feasible because of immobility, safety or critical illness and c) to monitor non–CPAP for OSA. Recently, telemedicine and Big data analysis is another growing field not only to monitor sleep and CPAP efficiency, but also as an indicator of distinguishing OSA phenotypes [16]. An issue of concern with telemedicine application is the adherence to strict professional and ethical standards. Finally, a night oximetry study can be used in carefully selected patients for screening purposes or re-evaluation.

TREATMENT OF SLEEP-DISORDERED BREATHING

Treatment of Obstructive Sleep Apnoea (OSA) should begin with the identification of modifiable lifestyle factors, such as dietary habits, sleeping position and alcohol use in the evening. Moreover, all patients with OSA should be counselled about the potential benefits of treatment and the hazards of going on without treatment.

Currently, the cornerstone of intervention for moderate to severe OSA is Continuous Positive Airway Pressure (CPAP) treatment. The fundamental cause of OSA is upper airway collapse and continuous positive airway pressure therapy (CPAP) is used to redress this collapse, working

as a pneumatic splint. CPAP may also improve functional residual capacity (by recruiting alveoli), reduce the work of breathing and improve hemodynamics in patients with heart failure, by reducing preload and afterload [17].

CPAP devices can be connected to different interfaces which can be nasal, oronasal, full-face or oral masks, depending on the patient's facial anatomy and comfort. Optimal CPAP use has previously been defined as use for >4 h for >70% of nights. A linear relationship has been shown between CPAP use and improvement in sleepiness and memory. Not surprisingly, the severity of OSA and high symptom burden are associated with better adherence, as is the presence of a supportive partner [18].

For mild OSA, simpler actions may be often used instead of CPAP, including changes in sleep position (avoidance of supine position), weight loss and oral devices. Oral appliances for the treatment of snoring and sleep apnoea include mandibular advancement devices (MADs) and the less common tongue-retaining devices [19].

NON-RESPIRATORY SLEEP DISORDERS

Non-respiratory sleep disorders include a large number of sleep complaints that appear to any sleep clinic and sometimes can be difficult to distinguish and properly treat. Therefore, the non-specialist should be able to recognize these entities and refer patients to a specialized sleep facility. Disorders such as insomnia are quite common and can overwhelm health services if they are not appropriately managed. Moreover, other common sleep disturbances in the modern era include shift working and jet-lag.

Insomnia

Insomnia is a complaint of dissatisfaction with either the duration or quality of sleep. Insufficient sleep duration may be due to difficulties initiating sleep, difficulties maintaining sleep, or early awakening [20]. The establishment of insomnia diagnosis requires three fundamental criteria: recurrent symptoms, adequate sleep opportunity and impairment of daytime functioning. For example, a student who has sleep deprivation because he keeps on studying late at nights and wakes up early is obviously lacking adequate sleep.

A poor night of sleep is a nuisance that everyone experiences at some time point. But insomnia requires persistent symptoms on most nights of the week. Sleep hygiene measures should be carefully assessed in patients complaining about insomnia. Daytime complaints consist of fatigue, impaired cognitive abilities (e.g. decreased memory and concentration) and mood disturbances (e.g. irritability). As these symptoms may persist for prolonged time periods, chronic insomnia may lead to complications such as decreased work productivity and family issues. Health-related quality of life can be impaired as well. Subsequent daytime sleepiness can pose a higher risk for motor accidents [21].

The evaluation of insomnia is founded on classical clinical principles, including a detailed patient history and examination, with special attention to sleep and waking functions. Firstly, the primary insomnia complaint is carefully addressed. Then, the circumstances and activities are assessed and scrutinized. Afterwards, day-to-day variability of complaints and the evolution of the time is important. A reliable scale for the evaluation of insomnia is the Athens Insomnia Scale which is widely used and has been validated for the Greek population [22].

In line with the many components that play a role in the causation and maintenance of insomnia, several treatment methods have emerged. The usefulness of different therapeutic modalities depends on contributing factors and illness time course. Prescription of hypnotics is a common and accepted practice for acute insomnia, but in chronic insomnia, the emphasis is on a nonpharmacological approach and hypnotic drugs can be used as adjuvant in this setting.

Recommendations on good sleep hygiene are a default step in the treatment plan and adherence to these instructions often results in better coping with the problem for some patients (Table 3). If the complaints persist, then a formal cognitive and behavioral therapy for insomnia CBT-I should be recommended [23].

Circadian rhythm disorders

Circadian rhythmicity has been demonstrated in humans and is important to maintain homeostasis, by regulating core body temperature and hormone secretion, including cortisol, prolactin and growth hormone [24].

Table 3. *Principles of sleep hygiene.*

Bedtime should be used for sleeping
Improve environment conditions (light, sounds)
Avoid large volume dinner and beverages before going to bed
Schedule stressful activities long time before bedtime
Avoid alcohol consumption and caffeine after 6pm

There is significant variation amongst people regarding preference to morning and evening activities (morning types vs evening types). Large studies have shown that people around the world prefer going to bed between 23.00 and 00.00 and getting up in the morning between 7.00 and 7.30, but there are variations between genders, age groups and countries [25].

Shift work

In the 24h modern society, there is an ongoing pressure for shift working that sometimes may be a burden for employees. Sleep and other health problems arising from working schedules outside normal daylight hours can result in shift work disorder. Shift working is generally well-tolerated, but some people seem to be vulnerable to developing problems, such as those aged >50 yrs, persons with a history of sleep disorders (e.g. sleep apnoea) or those with chronic diseases including epilepsy, diabetes and alcohol abuse.

Types of shifts detrimental to well-being include: 12h shifts that involve critical monitoring tasks, heavy physical labor or exposure to harmful substances. Moreover, more than 12h shifts in a row and shifts starting earlier than 07:00 h cause sleep issues [26].

Jet lag

The body clock may demonstrate inertia when trying to adjust to rapid environmental changes to time cues, and the most abrupt change is moving from one time zone to another by air travel. Jet lag includes different symptoms such as inappropriate daytime tiredness, insomnia, early awakening, impaired concentration, reduced appetite and enuresis.

Jet lag is supposed to be worse when travelling eastwards as the day is shortened to <24 h; while travelling westwards has the opposite effect. It is easier for people to phase delay than waking up earlier when going east. The severity of jet lag depends on number of time zones crossed, length of flight and innate adaptation to time changes.

Melatonin preparations may be helpful in people frequently travelling by plane to help adapt to the new time zone. But melatonin can also have side-effects as reduced alertness, headache and nausea [27].

CONCLUSIONS

Optimal sleep time varies in adults and depends on socioeconomic factors (work pattern, education, country) and personal preference. It has been shown that sleep restriction to less than 5h a night can cause impaired vigilance, memory deficit and altered mood. Increasing sleep opportunity up to 10h a night improves cognitive function. In general, a night sleep of 7.5-8.5 a night seems to be adequate for the general population [28].

Sleep and particularly good sleep is important for well-being and for the avoidance of developing systematic diseases. Sleep disorders should be carefully identified and addressed and targeted treatment must be provided by specialists in sleep medicine in the dedicated sleep facilities.

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