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Excessive somnolence

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Excessive somnolence can be quite a incapacitating manifestation, and is frequently neglected by physicians and patients. This article reviews the determinant factors, the evaluation and quantification of diurnal somnolence, and the description and treatment of the main causes of excessive somnolence.

UNITERMS: Excessive somnolence. Sleep apnea. Narcolepsy. Nocturnal myoclonias.

Excessive somnolence (ES), which may be defined as difficulty in maintaining the desired level of alertness, or as an excessive quantity of sleep, is a common complaint, prevalent in 0.5–5 percent of the general population.[1] Besides raising important problems in diagnosis and treatment, it is frequently neglected by the physician and even by the patient. This represents a serious risk, since ES may be a warning sign of a potentially lethal disease, sleep apnea syndrome. In addition, ES may incapacitate patients, cause social and family problems, job accidents and firings, and create problems at school.

The new classification of sleep disorders (ICSD)[2] includes more than 30 causes of ES (Table 1). Thus, in cases of ES complaints, the physician should carry out a thorough investigation in order to diagnose it properly. Therefore, it is relevant to discuss the determinant factors of ES, sleep history, and diagnostic methods of ES.

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DETERMINANT FACTORS OF ES

1. Quantity and/or quality of sleep

The intensity of ES is directly related to the quantity of nocturnal sleep.[3] Partial or total sleep deprivation causes daytime somnolence in normal individuals, as evaluated by the multiple sleep latency test. Furthermore, mild restrictions of sleep (*e.g.*, a 1-hour reduction in sleep per night) gradually accumulate, leading to a progressive increase in daytime sleepiness, which is reversed if the duration of nocturnal sleep is increased.[3]

Daytime sleepiness is also associated with the quality of nocturnal sleep.[4] Some sleep disorders (*e.g.*, sleep apnea syndrome, periodic limb movement disorder) are characterized by awakenings of short duration, recorded on the electroencephalogram. These awakenings do not

necessarily awaken patients. The crucial point is that they do not usually cause a shorter sleep period, but mainly a fragmented sleep, which results in ES.[4]

2. Age group

When evaluating a patient with sleep complaints, it is vital to consider the age group, since sleep patterns are known to change with the advance of age.[5,6] Certain age groups have clear sleep patterns that deserve to be mentioned, keeping in mind that individual variations occur within the same age group.

During adolescence, several physical, hormonal, and psychological changes occur, as well as changes in nocturnal sleep and daytime alertness.[5] Tanner 13[7] demonstrated that daytime alertness (as evaluated by the multiple sleep latency test) diminishes despite the same amount of nocturnal sleep; suggesting that the need for sleep increases in adolescence. Also, ES usually manifests as narcolepsy and idiopathic hypersomnia during the second decade of life.[2]

Billiard et al.[5] studied young men (17 to 22 years), and determined the prevalence and contributory factors of ES.[9] Around 5 percent of the interviewed persons reported that ES affected their daytime activities, and ES was associated with the use of hypnotics, insomnia (initial, intermediate and final), irregular sleep-wake cycles, snoring, and the number of hours of sleep (< 5 hours and > 11 hours). Also, the proportion of individuals with ES was higher among those who reported the presence of cataplexy (auxiliary symptom of narcolepsy). An interesting finding was the relationship between ES and the number of hours slept per night. A complaint of ES is not surprising when nocturnal sleep is reduced, however, a relationship between prolonged sleep and daytime somnolence is usually not expected. This would either represent a "hangover" due to excessive sleep, or a manifestation of a pathological process (e.g. idiopathic hypersomnia).

The elderly show several sleep pattern modifications, such as: an increase in sleep latency and the number of awakenings during the night; a decrease in delta sleep; and an increase in daytime naps.[10] In this population, the fragmentation of nocturnal sleep due to respiratory and motor disorders is an important factor responsible for ES.[11,12]

3. Circadian Rhythms

The sleep-wake cycle, in an adult individual, presents a two-phase pattern with two periods of sleep tendency, one at night, and other (less important), in the afternoon.[13] Thus for many individuals, in some countries, a daily nap after lunch is the rule.

Examples of ES due to rhythm disorders are seen in shiftworkers and people traveling quickly through different times zones (jetlag).

4. Drugs

Several drugs alter sleep patterns. Examples of drugs that induce ES are: benzodiazepines, barbiturates, H1-antihistaminics (diphenydramine), beta-blockers and alcohol.[4,14-16]

6. Illnesses

Table 1 lists the causes of ES according to the ICSD criteria.[2] As can be observed, ES may be due to psychiatric and respiratory disorders, central nervous system disorders, etc. Some disorders will be discussed later on.

PATIENT'S SLEEP HISTORY

The presence of ES demands a complete "survey" of the 24-hour activities of the patient. The time that the patient goes to bed; sleep latency (how long the patient takes to fall a sleep); number of awakenings during the night; time the patient wakes up completely; and quality of sleep (during working days, as well as on weekends and vacations) must all be investigated. It is important to ask about the various situations in which (e.g., television watching, reading, meetings, car driving, etc.) and the times in which sleepiness occurs. Daytime naps should be investigated in regard to the time and frequency of occurrence, quality (repairer or not), and the occurrence of dreams.

The somnolent patient usually reports sleeping one or more times during the day, many times in unusual situations. Rituals to "repel ES" are frequently developed, such as: washing the face with cold water, painful maneuvers, and the use of caffeine. Moreover, the patient may refer to somnolence as fatigue, loss of energy, or prostration. The inverse may also occur, with the patient interpreting fatigue as somnolence. The patient may even deny the symptoms, either because he has already incorporated them as habits (e.g., "I do not have a sleep problem since I sleep in any place") or because ES might be interpreted as laziness or indolence. A sleep log, kept

Table 1
Causes Of Excessive Somnolence (ES)

1. Behavioral/Psychophysiologic Disorders:
- Inadequate sleep hygiene
- Insufficient sleep

2. Psychiatric Disorders:
- Mood disorders
- Alcoholism

3. Environmental Factors:
- Environmental sleep disturbance
- Toxin-induced sleep disturbance

4. Drug Use

5. Respiratory Disorders During Sleep:
- Obstructive Apnea Sleep Syndrome (OASS)
- Central Apnea Sleep Syndrome
- Central Alveolar Hypoventilation Syndrome
- Neurogenic tachypnea related to sleep

6. Movement Disorders:
- Periodic limb movement disorder

7. Alterations of Sleep-Wake Cycle:
- Long periods of sleep
- Time zone changes
- Shiftworkers
- Delayed phase of sleep phase
- Advanced phase of sleep phase
- Non 24-hour sleep-wake cycle
- Irregular sleep-wake pattern

8. Disorders of the Central Nervous System:
- Narcolepsy
- Idiopathic hypersomnia
- Posttraumatic hypersomnia
- Recurrent hypersomnia
- Fragmented myoclonias
- Subvigil syndrome
- Parkinson's Disease
- Dementia
- Sleeping sickness

9. Other Causes of ES:
- Sleep disorders associated with menstruation
- Sleep Disorders associated with pregnancy

during some weeks (2 or more), may be useful, especially in circadian rhythm disorders.

The age that symptoms began may furnish important information. For narcolepsy, ES usually starts during the second decade of life; for sleep apnea syndrome (although ES may occur in any age group), occurrence is more common in men after 40 years, and in women after menopause.

Some additional symptoms may help determine the cause of somnolence, such as: snoring, respiratory arrests during sleep, morning headaches, cataplexy, hypnagogic hallucinations, sleep paralysis, and automatic behavior.[17]

An interview with bed partners and relatives is useful to obtain data about the nocturnal behavior of the patient. Obviously, a general clinical history of the patient should be obtained and, when necessary, an evaluation by other specialists.

METHODS FOR QUANTIFICATION AND DIAGNOSIS OF ES

The quantification of ES is complex and may include objective and subjective measures. The subjective evaluation encompasses the presence of behavioral signs – such as: yawning, palpebral ptosis, alertness lapses, rubbing of the eyes, shaking of the head, etc.– and methods for self-evaluation, such as: the Stanford Sleepiness Scale,[18] visual-analogical scales19 and the Epworth Sleepiness Scale.[20]

Pupillometry is a method for objective evaluation, since the pupillary diameter is an index of autonomic activity, and constriction occurs during sleep.[21]

The test of multiple sleep latency[22] is the most used examination for objective quantification of daytime somnolence. Four to five polygraphic readings are taken during the day, at 2-hour intervals, lasting 20 minutes.

During each reading, the time that the patient takes to fall asleep is measured, and the mean sleep latency is calculated (values below 5 minutes are considered abnormal). This test, besides quantifying the severity of ES, also detects the presence of early REM sleep, which is important for the diagnosis of narcolepsy. Some basic precautions should be considered when carrying out this test, such as: suspending the use of some drugs (tricyclic antidepressants, monoamine oxidase inhibitors, stimulants, sedatives, hypnotics, antihistamines) at least 14 days prior to the examination; maintaining a regular sleep-wake cycle one week before; and performing a sleep polygraph the night before the test.[1]

A laboratory sleep evaluation, or sleep polygraph, is recommended to evaluate nocturnal sleep in patients complaining of ES. The patient sleeps one or more nights at the sleep laboratory, and several parameters are evaluated (electroencephalogram, ocular movements, muscular activity, respiration, arterial oxygen saturation, electrocardiogram, etc). A preliminary interview with the sleep polygraphist is essential to evaluate the patient's history, sleep habits, and use of drugs that could interfere with results (e.g. antidepressants, hypnotics, anxiolytics), thus preparing each patient for the examination. This test is not necessary when ES is clearly secondary to chronic sleep deprivation or to drug use.

SOME DISEASES THAT CAUSE ES ARE DISCUSSED BELOW

1. Sleep apnea syndrome

Sleep apnea is defined as an arrest of the air passage through the upper respiratory airways (URA) for longer than 10 seconds.

Three types of respiratory arrests are:

1. Central apnea: a complete respiratory arrest occurs.
2. Obstructive apnea: an obstruction of air passage through the URA occurs, with persistence of the respiratory effort.
3. Mixed apnea: the arrest is initially central and evolves to obstructive.

Sleep hypopneas are also described, and are characterized by a 50-percent decrease in air flow, 4-percent decrease in arterial oxygen saturation, and the awakening of the patient.

These events may cause insomnia or ES; central apnea is usually associated with complaints of insomnia, and obstructive apnea is associated with hypersomnia.

2. Obstructive Apnea Sleep Syndrome (OASS)

Obstructive Apnea Sleep Syndrome (OASS) is characterized by repetitive episodes of URA obstruction which occur only during sleep.The obstruction may be the result of any factor that increases the resistance of the URA, causing the occlusion of the oropharynx.[23] Therefore, many conditions may predispose or aggravate OASS, such as: adenotonsillar hypertrophy; macrognathia; micrognathia; retrognathia; obesity; tumors; polyps; nasal obstructions; allergic rhinitis; hypothyroidism; acromegaly; chronic obstructive pulmonary disease; restrictive pulmonary diseases; neuromuscular diseases affecting the thorax (e.g., poliomyelitis, kyphoscoliosis, myotonic dystrophy); alcohol consumption or nervous system depressants.[24]

During obstruction, a reduction in arterial oxygen saturation occurs, with an increase in pCO_2 and systemic and pulmonary arterial pressure; cardiac arrhytmias also occur (bradycardia-tachycardia, asystolia, atrioventricular block, etc.).[25] These alterations, which may be of variable severity, activate structures in the brainstem that cause the patient's awakening with the return of respiratory reflexes. The sudden opening of the URA causes a characteristic inspiratory snore.

Patients complain about ES, which may be very incapacitating. Fatigue, mental confusion upon awakening, morning headaches, memory disorders, depression, irritability, sexual impotence, and nocturnal enuresis may occur. During sleep, snoring is quite loud, being interrupted by pauses (apneas) of varying duration. Excessive movement may also occur.[26]

Although it may occur in any age group, OASS is more commonly observed in middle-aged males. If not treated, it may cause systemic arterial hypertension, pulmonary hypertension, cor pulmonale, polycythemia, cardiac arrhytmias, or even death while sleeping.[26]

Diagnosis is obtained by using a sleep laboratory evaluation that monitor and cardiorespiratory variables and records the periods of obstruction, and the disturbances of cardiac rhythm and of arterial oxygen saturation.[27] The choice of treatment requires an analysis of the factors responsible for obstruction, and an evaluation by an ear,nose and throat specialist, a pneumologist, and an endocrinologist.

The therapeutic possibilities for OASS include:

1. General approach: avoid depressants of the central nervous system (hypnotics, anxiolytics, alcohol);[26,28] avoid sleeping in the horizontal supine position;[29]
2. weight loss,[30] when necessary;
3. drug treatment with variable results:
   a) tricyclic antidepressants - for mild to moderate cases;
   b) medroxyprogesterone acetate - for patients with hypercapnia;[31, 32]

4. a mask for continuous positive air pressure (nCPAP):[33-36] with the use of a nasal mask, the URA are kept open using low pressure levels (5-18 cm H_2O); it has been the preferred treatment for moderate to severe cases;
5. removable oral devices;[37-41]
6. surgery: uvulopalatopharyngoplasty,[42, 43] tonsillectomy and adenoidectomy,[44] nasal surgery,[45] tracheostomy (rarely),[46] or mandibular and/or maxillofacial surgery.[47]

3. Upper Respiratory Airways Resistance Syndrome

Although this disorder is not shown in the ICSD Table, it was recently described[48] and deserves to be discussed. Some patients who snore loudly while sleeping and are sleepy during the day do not show OASS. The laboratory sleep evaluation shows, however, a fragmentation of secondary sleep and brief awakenings associated with abnormal respiratory effort, measured by esophageal pressure. These abnormal efforts are associated with the snoring, and remission of excessive somnolence may be obtained by using the nasal CPAP.

4. Periodic Limb Movement Disorder

This disturbance, also known as nocturnal myoclonias, is characterized by the occurrence, during sleep, of repetitive and stereotyped movements that mainly affect the lower limbs. These movements, which last 0.5-5 seconds and are usually repeated at intervals of 20-40-seconds, occur uni- or bilaterally and are characterized by foot dorsiflexion, toe extension and partial flexion of the knee, and sometimes, of the hip.[49] They should not be confused with massive muscular disturbances, which occasionally acompany the sensation of "falling into space" that occurs during the wake-sleep transition.

Myoclonia episodes may last from minutes to hours, leading to complaints of insomnia (frequent awakenings during the night) as well as ES.[50] They can be related to or aggravated by several medical conditions, such as chronic uremia, diabetes and other metabolic diseases, the use of tricyclic antidepressants and monoamine oxidase inhibitors, and the interruption of hypnotics and anticonvulsants.[2] The pathophysiology of this disorder is unknown, as is its natural history. Prevalence increases with the age.[11]

Proper diagnosis is obtained using a sleep laboratory evaluation and by monitoring the activity of the tibialis anterior muscle. Drugs used for treatment include: clonazepam (0.5-2 mg at night);[51] dopamine (carbidopa/L-dopa1:4; benzerazide/L-dopa 1:4)[52, 53] and opiates.[53, 54]

5. Narcolepsy

Narcolepsy is an ES disorder of unknown causes acompanied by auxiliary symptoms (cataplexy, hypnagogic hallucinations, sleep paralysis) which reflect dissociated fragments of REM sleep.[2] About 20-25 percent of narcolepsy patients have all these symptoms.[55]

Daytime sleepiness is usually the first symptom, and is characterized by continuous somnolence or "irresistible sleep attacks," and by daytime naps of variable duration which are restoring (after the nap the patient feels more alert for some hours).[56] Frequently, patients refer to the occurrence of dream during the naps.

Cataplexy is practically pathognomonic of narcolepsy. It is characterized by a sudden loss of muscular tonus of one or more muscular groups, and is always precipitated by an abrupt emotion. The duration is usually short, varying from a few seconds to minutes, alertness is preserved, and patients may present perception disturbances. It is a quite incapacitating symptom and occurs independently of sleep episodes, although these may occur following a caplectic crisis. About 70 percent of patients with narcolepsy have cataplexy.[2]

Hypnagogic hallucinations are quite realistic perception experiences, usually visual, that occur during the wake-sleep transition (they are denominated hypnopompic when they occur during full awakemess). Patients report feeling intense fear during these episodes, which occur in 50 percent of narcolepsy cases.

Sleep paralysis is a general transitory incapacitation of the organism to move, which occurs at the beginning or end of sleep. These episodes, described by the patients as terrifying, last from one to several minutes, and occur in 50 percent of the cases of narcolepsy and in 5 percent of normal individuals. The narcolepsy patients also complain about insufficient nocturnal sleep, with frequent awakenings.

Because this is a chronic disease without significant remission or a definitive treatment, the diagnosis should be carried out with extreme caution. A laboratory sleep evaluation and multiple sleep latency test are indicated.

The treatment is symptomatic and includes:[55]

1. Education of patients and relatives.
2. Adequate sleep hygiene, with a regular sleep scheme and scheduled daytime naps.
3. Psychological assistance.
4. Stimulants to control ES:
   - methylphenidate: 5-60 mg/day

- dextroanfetamines: 5-60 mg/day
- pemoline: 18.75-112.5 mg/day
- mazindole: 3-6 mg/day

These drugs may be prescribed for daily usage or according to the patient's needs (in situations that require alertness), and should be avoided during weekends and vacations, to inhibit the development of tolerance.

5. Tricyclic antidepressants to control cataplexy:
   - imipramine: 25-100 mg/day
   - chlomipramine: 25-100 mg/day

6. Idiopathic Hypersomnia

Idiopathic hypersomnia Is characterized by a persistent complaint of ES, presumably due to a central nervous system disorder.[2] Nocturnal sleep is usually long (> 8 hours), and daytime naps are prolonged (1-2 hours), but not repairative. It occurs usually in adolescence and during the third decade of life.

Auxiliary symptoms may include migraine crises, headaches, fainting, and Raynaud's phenomenon, which suggests a dysfunction of the autonomic nervous system.[57] A laboratory sleep valuation does not evidence any abnormality, except for periods of prolonged sleep.[9] The multiple sleep latency test reveals latencies shorter than 10 minutes in the absence of REM sleep. It is a chronic disease, with a partial therapeutic response to stimulants, tricyclic antidepressants and monoamine oxidase inhibitors.[58]

7. Recurrent Hypersomnia

The most well-known type of recurrent hypersomnia is Kleine-Levin's syndrome.[59] It is a rare disorder, characterized by periods of ES, lasting days to weeks, occurring at intervals of months or years. The symptomatic phase is characterized by prolonged sleep (18-20 hours/day) associated with overeating and psychiatric symptoms (depression, anxiety, hyper or hyposexuality, hallucinations). In the atypical form, overeating does not occur. Patients are normal during the intervals.

Recurrent hypersomnia usually begins during the second or third decades of life and seems to have a benign evolution, disappearing after some time of illness.[2] Even though there is no specific treatment, there are reports of satisfactory responses to central nervous system stimulants, tricyclic antidepressants, and lithium carbonate.[59]

Periodical hypersomnia associated with menstruation[60] usually occurs at the end of the menstrual period and lasts for some days, and may be accompanied by overeating and sexual behavior disorders. The pathophysiology of this disorder is unknown and the treatment is achieved with anovulatories.

8. Posttraumatic Hypersomnia

Posttraumatic hypersomina is defined as excessive sleepiness that occurs following cranio-encephalic trauma.[2] This ES is usually associated with other symptoms, such as headaches, fatigue, difficulty in concentrating, memory disorders, and psychiatric disturbances.

9. ES Associated With Psychiatric Disturbances

Some patients present ES and daytime naps in stressful situations. Usually, the episodes are of short duration, becoming less intense with the disappearance of the causative factor.

In mood disorders, insomnia is the most common complaint, but ES may also occur, especially in bipolar disturbances, and in the so-called atypical depressions, with the inversion of the normal pattern: increase in the total time of sleep, afternoon deterioration, increase in appetite and weight.[61]

10. ES Associated With Clinical Diseases

ES may be associated with metabolic disorders, such as diabetes, hypothyroidism, uremia, hepatic failure, and infectious diseases. The manifestation of somnolence is quite variable in these conditions, and other signs and symptoms usually predominate.

11. Insufficient sleep

Many persons sleep less than they need to, either because of social pressure or by their own initiative. This situation causes ES, but is reversed when the individual sleeps normally again, e.g., on weekends or during vacations.

RESUMO

Sonolência excessiva pode ser uma manifestação bastante incapacitante, sendo freqüentemente negligenciada pelo médico e pelo paciente. Este artigo é uma revisão sobre os fatores determinantes, a avaliação e a quantificam de sonolência diurna, e a descrição e o tratamento das principais causas de sonolência excessiva.

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