NAMS Regional Symposium on Sleep Medicine
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CAUSES OF HYPERSOMNIA – NARCOLEPSY

SYNOPSIS

Volitional sleep deprivation and obstructive sleep apnea are the most common causes of hypersomnia. The remaining causes are primarily due to primary central nervous system abnormalities, the most common of which is narcolepsy, a primary disorder of the neural control of wakefulness and sleep.

Narcolepsy is the prototypic example of dissociated sleep-wake phenomenon in which components of one state (REM) appear in another (wakefulness). Narcolepsy is a relatively frequent disorder with a prevalence of 0.09%. A clear genetic component is indicated by the fact that over 90% of individuals with narcolepsy carry the HLA DR15 and HLA DQ6 gene, which is found in less than 30% of the general population. Siblings of individuals with narcolepsy have a 60-fold increased likelihood for developing the disease. Narcolepsy is thought to result also from abnormal neurotransmitter functioning and sensitivity and abnormal immune modulation. Clinical manifestations of normal sleep include (i) Excessive Daytime Somnolence (EDS); (ii) Cataplexy; (iii) Hypnogogic hallucinations; and (iv) Sleep paralysis. Whenever possible, the diagnosis of narcolepsy should be confirmed by polysomnography (PSG) followed by a multiple sleep latency test (MSLT).

Cataplexy:

Cataplexy, which occurs in 65% to 70% of the patients of narcolepsy, comprises of sudden loss of muscle tone, typically triggered by emotion such as laughter, anger, excitement, delight or surprise. The muscle weakness of cataplexy may be complete, resulting in the patients falling or being forced to sit; much more commonly, the weakness is milder and more focal, taking the form of facial sagging, slurred speech or localized weakness of an extremity. Cataplexy may never occur in 30% of patients with narcolepsy or may precede the onset of EDS. To reiterate, the salient features of Cataplexy are : (i) if severe and generalized, cataplexy may cause a fall ; (ii) more subtle forms exist with only partial loss of tone (eg., head nod and knee buckling);

(iii) respiratory and extraocular movements are preserved; and (iv) cataplexy is usually triggered by emotions (especially laughter and anger)

Sleep Paralysis:

Sixty percent of individuals with narcolepsy experience sleep paralysis upon awakening from REM sleep (usually from a dream). This at times frightening manifestation consists of total-body paralysis, with sparing of respiration and of eye movements, lasting from seconds to minutes.

The salient features of Sleep paralysis are: (i) usually the patient is unable to move upon awakening; (ii) less commonly, the patient is unable to move upon falling asleep with consciousness intact; (iii) paralysis is often accompanied by hallucinations; (iv) respiratory and extraocular muscles are spared; (v) paralysis occurs less frequently when the person sleeps in an uncomfortable position; and (vi) paralysis can be relieved by sensory stimuli (eg., touching or speaking to the person).

The following are also common features of narcolepsy : (i) a tendency to take short and refreshing naps during the day, these may be accompanied by dreams; (ii) trouble sleeping at night; (iii) nocturnal compulsive behaviours (sleep related eating disorder and nocturnal smoking); and (iv) obesity.

In children, the features of Narcolepsy are: (i) restlessness and motor over activity may predominate; (ii) academic deterioration, inattentiveness and emotional liability are common; (iii) at disease onset, children with narcolepsy and cataplexy may display a wide range of motor disturbances that do not meet the classic definition of cataplexy; (iv) motor disturbances may be negative (hypotonia) or active; and (v) motor disturbances may resolve later in the course of the disorder.

Diagnosis:

The DSM-5 defines narcolepsy as recurrent episodes of irrepressible need to sleep, lapsing or napping occurring within the same day. These must have been occurring at least three times per week over the past 3 months. There must also be presence of atleast one of the following : (i) episodes of cataplexy occurring at least a few times per month; (ii) hypocretin deficiency; and (iii) REM sleep latency < 15 minutes or a mean sleep latency < 8 minutes and two or more sleep-onset REM periods (SPREMPs).

Narcolepsy can be categorized as mild, moderate or severe based on the frequency of cataplexy, need for naps, and disturbance of nocturnal sleep. In addition, the DSM-5 identifies five subtypes including (i) narcolepsy without catraplexy but with hypocretin deficiency; (ii) narcolepsy with cataplexy but without hypocretin deficiency; (iii) autosomal dominant cerebellar ataxia, deafness and narcolepsy; (iv) atuosomal dominant narcolepsy, obesity and type 2 diabetes; and (v) narcolepsy secondary to another medical condition.

Whenever possible, the diagnosis of narcolepsy should be confirmed by polysomnography (PSG) followed by a multiple sleep latency test (MSLT).

Pathophysiology:

Narcolepsy is thought to result from genetic predisposition, abnormal neurotransmitter functioning and sensitivity, and abnormal immune modulation. Current data indicate certain human leukocyte antigen (HLA) subtypes and abnormal hypocretin (orexin) neurotransmission, which leads to abnormalities in monoamine and actylcholine synaptic transmission, particularly in the pontine reticular activating system.

Management:

Treatment of Narcolepsy has both nonpharmacologic and pharmacologic components. Sleep hygiene is important. Pharmacologic treatment of narcolepsy involves the use of central nervous system stimulants such as methyphenidate, modafinil, dextroamphetamine sulphate, methamphetamine and amphetamine. These medications help reduce daytime sleepiness, improving the symptom in 65% to 85% of patients.

SUGGESTED READING

1. American Academy of Sleep Medicine. International Classification of Sleep Disorders., 2 nd edition. Darien, IL: American Academy of Sleep Medicine: 2005.
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4. Lockrane B, Bhatia P, Gore R (2005). Successful treatment of narcolepsy and cataplexy. A review. *Can Respir J.* **12**: 225 – 227.
5. Guilleminault C, Pelayo R (1998). Narcolepsy in prepubertal children. *Ann Neurol*. **43**: 135 – 142.