

Narcolepsy and Community Safety

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ABSTRACT

Narcolepsy is one of the risk factors to excessive day sleepiness (EDS). Narcolepsy with sleep apnea contribute to 75% of the causes of EDS, and 71% of all sleep-related accidents(1). Narcolepsy is responsible for traffic accidents regardless of age, sex, and marital status or to socioeconomic factors(23). Early diagnosis, treatment, behavioral and lifestyle changes will help in the reduction of the impact of this neurological disorder. There is no known way to prevent narcolepsy. Only treatment and avoidance of the conditions that trigger or aggravate the disease may reduce the number of attacks(10). Fundamental control measures and assessment can help to understand and reduce episodes and long term consequences of narcolepsy's impact.

Keywords: Narcolepsy, Cataplexy, Sleep disorders, Community, Safety, Precaution, Prevention.

INTRODUCTION

Our modern life requires us to rush. This means we are in a continuous, speedy day life. We rush to catch meetings; we eat fast food, and don't exercise enough. Meanwhile, we are working different and longer shifts, even working two jobs. Transportation is the main way to commute and go to work every day. Time is the operator to our schedules, along with this stressful life style we abandon our health to sleep enough hours. Ultimately, people fall asleep at work, for example air traffic controllers, and are endangering their lives and others, and affecting their quality of life due to a lack of functionality. Narcolepsy is one of the risk factors to excessive day sleepiness (EDS). Narcolepsy with sleep apnea contribute to 75% of the causes of EDS, and 71% of all sleep-related accidents⁽¹⁾. Narcolepsy is responsible for traffic accidents regardless of age, sex, and marital status or to socioeconomic factors⁽²³⁾. Early diagnosis, treatment, behavioral and lifestyle changes will help in the reduction of the impact of this neurological disorder.

WHAT IS NARCOLEPSY?

Narcolepsy is a chronic neuro-degenerative disorder caused by deficiency of "orexin" (or hypocretin)-producing neurons in the lateral hypothalamus⁽⁶⁾. Causing our brain to be unable to control sleep-wake cycles. People with narcolepsy are experiencing an urged desire to fall asleep while they are working, talking, or eating. Episodes last from a few seconds to

several minutes, most dangerously when they are driving an automobile or operating machinery. Normally, we progress through cycles of sleep stages before or after we leave the state of sleep known as rapid eye movement (REM). In the case of narcolepsy the sleep pattern we may skip some or all of the sleep stages that cause the person to fall in REM immediately or to awaken from it⁽¹⁰⁾.

CAUSES

The mystery behind the dysfunction of the hypothalamus, or REM sleep-regulating pathways, finally was solved in the last few years including orexin which was discovered in 1998⁽¹¹⁾. Orexin is responsible for regulating sleep-wake cycles. Gene alteration was involved by considerable evidence in the orexin deficiency which is enough to induce narcolepsy. Unraveling the mystery is not an easy task; most of the cases are acquired during adulthood, so scientists think that narcolepsy is not only about genetics although it is main cause. Approximately, in 90% of narcolepsy cases there are human leukocyte antigen DQB1* 0602 and DQA1 * 0102 which makes many researchers believe it is immune-mediate disorder⁽⁶⁾. Infections, trauma, hormone change and stress may also cause this sleep disorder⁽¹⁹⁾.

SYMPTOMS

There are four main symptoms (classic tetrad) which were first described by Yoss and Daly in

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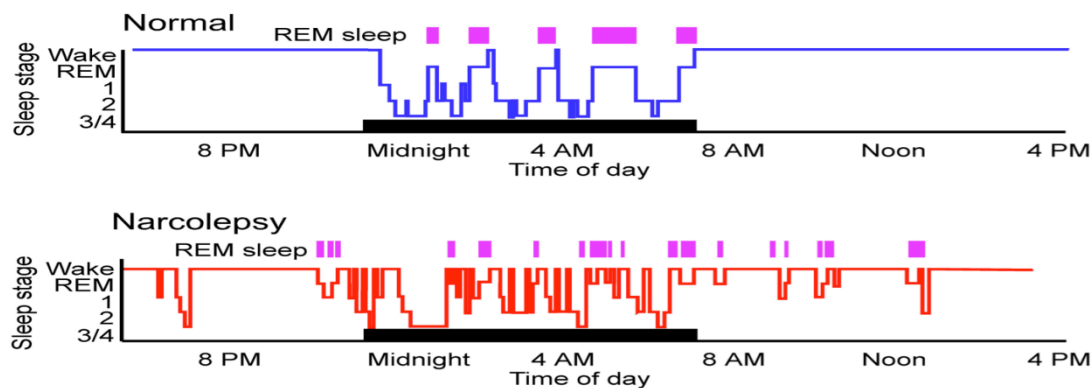
1950s.

Excessive Day Sleepiness (EDS):

Mostly all patients with narcolepsy experience EDS and it is first symptom to appear clinically.

Cataplexy:

Occurs in 70% of all patients with narcolepsy⁽¹⁹⁾, characterized by sudden and temporary loss of muscle tone due to the brain abruptly entering REM stage. In about 10% of all cases, cataplexy is the first symptom that patient to experience, and it could be misdiagnosed as a seizure attack. Cataplexy is triggered by laughter, excitement or anger⁽¹⁰⁾.



(Person with narcolepsy has fragmented sleep, a rapid entry into REM sleep, and numerous naps during the day that include REM sleep as compared to healthy individual, Source: BIDMC Neurology, Harvard medical school, 2017)

EPIDEMIOLOGY

First described by Gelieneau in 1880 and by Westphal in 1887⁽⁹⁾, narcolepsy with cataplexy affects about one in every 3,000 Americans, 3-5 per 10 000 of European populations⁽³⁰⁾, one per 500,000 in Israel, and about one per 600 in Japan. Thus it is not a rare disorder but it is under diagnosed, a typical patient is symptomatic for 10 years before the diagnosis is established⁽¹⁶⁾. It affects male and female equally, and could start as early as childhood, adolescent and adult hood, and once it appears it is present for life⁽¹⁰⁾,⁽¹⁹⁾. Narcolepsy can run in families, it is estimated up to 10% of diagnosed narcolepsy with cataplexy patients have a close relatives who have same symptoms. Risk of developing this disorder by close relatives of narcoleptic patients is higher than those of general population⁽¹⁹⁾. Narcolepsy is not a rare disorder, but sometimes it takes years to be diagnosed. Cataplexy cases have been misdiagnosed as pseudoseizure, and psychiatric issues such as conversion disorder, malingering, and psychosis⁽⁵⁾.

Sleep Paralysis:

It is temporary loss of muscle power in movement and speech, at the end of the event the person will recover muscle power.

Hypnagogic Hallucinations:

These are dreamlike images during the awake state instead of during sleep time.

In about 60% of narcolepsy cases, people have both EDS and cataplexy⁽¹⁰⁾ other symptoms such as *Disrupted nocturnal sleep* and *Obesity* may be experienced.

Dangerous Incidents

- In August, 2007, a police dispatcher in Chicago area told her supervisor that she had narcolepsy and she was fired⁽⁸⁾.
- On Feb, 19, 2011, an air traffic controller at McGhee Tyson Airport in Knoxville, Tenn. went to sleep for 5 hours during the midnight shift⁽⁴⁾.
- In March, 2011 another air traffic supervisor at Washington's Regan National airport dosed off at his midnight shift⁽⁴⁾. The last two incidents narcolepsy was not confirmed as the cause but rather sleepiness in general, which may be a symptom of narcolepsy.

DIAGNOSIS

Clinical examination and medical history are very essential in considering narcolepsy by doctors. Cataplexy mostly is a specific sign and rarely present in other disorders. In contrast, EDS could be present in wide ranging list of diagnoses, such as : sleep apnea, some viral or bacterial infections, depression, chronic illnesses such as anemia, congestive heart failure, restless leg syndrome, fibromyalgia and

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rheumatoid arthritis that disrupt normal sleep patterns, consumption (alcohol, caffeine, nicotine), and sleep deprivation⁽¹⁹⁾.

There are two main tests that should be performed in a sleep disorder clinic to confirm the diagnosis:

Polysomnogram (PSG): where the patient spends the night at the sleep center and the result aims to reveal if REM occurs in abnormal times during normal sleep cycle.

Multiple sleep latency test (MSLT): The patient is asked to come back during the day to document their tendency to fall asleep during waking hours by proving that they enter REM during abnormal times. MSLT is conclusive if REM either begins immediately or within a few minutes of sleep onset during at least two of the scheduled naps⁽¹⁹⁾.

Other tests may be helpful in some cases:

Gene profile: to measure the human leukocyte antigen⁽¹⁹⁾, also it may have successful future therapies like orexin gene therapy, transplantation of orexin neurons, stem cell precursors or engineered cells to produce orexin peptides⁽⁶⁾.

CSF (Cerebrospinal fluid) sampling: to identify definitely the lack of orexin.

TREATMENT

Narcolepsy cannot be cured and does not go away, but it is not a progressive disease. Only medications, behavioral and life style changes can diminish the symptoms and consequential injuries.

Drug Management

Currently, Stimulants can treat sleepiness while Antidepressants can treat Cataplexy and other abnormal REM sleep (sleep paralysis, hypnagogic hallucination), or both EDS and cataplexy by sodium oxybate^{(13), (14), (15)}.

Stimulants: (e.g.: *Modafinil/Armodafinil, Methylphenidate, and Amphetamine*).

These drugs are considered first line therapy because of the low cost, availability and higher efficacy, but can lead to tolerance and abuse with some negative side effects like irritability, insomnia, headache, anxiety.

Antidepressants

- Tricyclic antidepressants (TCA): (e.g.: *Clomipramine, Amitriptyline, Imipramine*)

- Selective serotonin reuptake inhibitors (SSRIs): (e.g.: *Fluoxetine, Paroxetine, Sertraline*)
- Selective norepinephrine reuptake inhibitors (SNRIs): (e.g.: *Duloxetine, Venlafaxine*)

Side effects may include dry mouth, headache, constipation, and blurred vision.

Sodium Oxybate

As hypnotic compound is approved by FDA to treat both EDS and cataplexy, but should be reduced or discontinued if there are side effects such as enuresis, excessive sedation that interferes with safety^{(13), (15), (16)}.

Pitolisant

Pitolisant is an inverse agonist of the histamine H3 receptor, thus increasing histaminergic tone in the wake promoting system of the brain⁽¹⁵⁾. Currently, pitolisant is only approved in Europe to treat narcolepsy since 2016. Pitolisant was found to be almost as good as modafinil for the relief of excessive daytime sleepiness. When the two were compared, pitolisant had a much better safety profile. As modafinil is potentially addictive, thus pitolisant does not appear to have abuse potential^{(17), (18)}.

Behavioral and life style changes

The goal is to maintain good, quality nighttime sleep that can reduce EDS and fatigue the next day⁽¹⁹⁾, so the patient feels refreshed and comfortable to start his or her daily performance. Among these essential measures⁽¹⁹⁾:

- Maintain regular sleep pattern every night.
- Maintain regular exercise and meal schedule before bedtime
- Avoid alcohol, caffeine, and smoking at night.
- Bedroom must be warm with more comfy bed.
- Several short daily naps (10-15 minutes).

Impact of Narcolepsy

Narcolepsy is a medical disorder whether it is undiagnosed or untreated. It is endangering not only the patients themselves but also other innocent victims as with bus, or occupational drivers, factory workers, air traffic controllers or police dispatcher, etc. So the impact is growing with faster industrialization and the rush of everyday life. According to Federal Motor

Carrier Safety Administration report, stating that there is an increased risk for a motor vehicle crash by narcoleptic drivers (Relative Risk = 6.15, 95% CI 3.50, 10.78) when compared to other drivers who do not have narcolepsy. The report also emphasizes that the vast majority of

those drivers who are on treatment do not return to normal levels of day time sleepiness⁽²⁷⁾. Another serious impact of narcolepsy is seen in untreated elderly patients with narcolepsy are suffering from multiple falls which are causing significant morbidity and mortality at their age⁽¹²⁾.

Narcolepsy significantly affects the quality of life, education and work⁽²⁾, resulting in impaired social and recreational activities, increased human errors and loss of productivity⁽⁶⁾. Individuals who suffer from narcolepsy are experiencing major socioeconomic consequences, high rate of unemployment, lower income, and as a chronic disorder its medications cost patients a significant amount of money for the rest of their life⁽²⁴⁾. Narcoleptic individuals have an association with obesity, and are correlated with higher risks of type 2 diabetes mellitus, cardiovascular disease, and migraine or other types of headache⁽⁹⁾.

PREVENTION

There is no known way to prevent narcolepsy. Only treatment and avoidance of the conditions that trigger or aggravate the disease may reduce the number of attacks⁽¹⁰⁾. Fundamental control measures and assessment can help to understand and reduce episodes and long term consequences of narcolepsy's impact.

Public Health Awareness

Public health awareness can be contributed by three main groups:

- Patient education about the danger of the consequences of untreated narcolepsy, seeking early treatment will reduce the impact. Follow the physician instructions and stick to behavioral strategies that are needed beside medications. Employees who suffer from frequent episodes need to inform their employer regarding work safety. Stop smoking and driving in hard to control or extreme cases. Avoid medications that have residual effects the following day including sleepiness and reduced alertness such as benzodiazepines⁽²¹⁾.
- Local media can alert the community about the potential risks of under diagnosed or

undertreated narcolepsy especially drivers and air traffic controllers. It remains rare enough that many individuals do not know about it nor know when or where to get tested.

- Physicians in general need to be more interested about sleep disorders such as narcolepsy and sleep apnea and their impacts if not treated, by referring more suspected patients to sleep disorder centers. Psychiatrists should consider narcolepsy in the differential diagnosis when refractory psychosis (e.g. schizophrenia) is emerging due to symptoms overlap⁽²⁵⁾. Parkinson's patients must be warned when they are taking bromocryptine, lisuridepergolide or piribedil because they induce sleep attacks as unwanted side effects⁽⁷⁾.

Fitness to Drive

There is a need for national and global systemic investigations for the presence of daytime sleepiness as a determinant of driving accidents⁽²²⁾. The regulations and guidelines dealing with fitness to drive regarding patients with sleep disorders should be reviewed in all the 50 states and countries around the world⁽²⁰⁾. Such regulations are different in all states, and the world. Because the goal of prevention is the avoidance of the conditions that trigger narcolepsy so we need to see clear and uniform regulations to address that issue, so we need more uniform standards. Assessment for the impact of these regulations is very important.

Support Groups

Living with the stigma of narcolepsy especially, with cataplexy has a negative impact on affected individual's self esteem, social integration, functional performance and education. Support groups can be extremely beneficial in coping and relieving stress and anxiety.

Work Place Safety and Adjustment

Narcoleptic patients can work in almost any type of job with flexible work schedules, coworkers' interactions, no driving required, and are closer to home. Employers must identify sleepiness at work as suspicious symptoms of narcolepsy until proven otherwise. For many years fatigue, extended shift work or lack of sleep were blamed for EDS. Workers have been afraid to admit of having narcolepsy or some of its symptoms because they might lose their jobs. The guidelines recommend disqualifying a commercial motor vehicle driver

with narcolepsy regardless of treatment⁽²⁸⁾. Americans with Disability Act (ADA) requires employers to reasonably accommodate the needs of their workers like with narcolepsy by allowing them to take short naps during the workday or adjust work schedule to avoid sleepy periods⁽²⁶⁾.

Health Care Access

For those poor, unemployed people should be considered at higher risk of undiagnosed narcolepsy because they have difficulty getting health care access. Social security disability insurance or supplemental security income programs may offer financial help for those who are not able to work after being diagnosed with narcolepsy.

Further Investigation and Mentoring to H1N1 Vaccine

Early this year WHO's Global Advisor Committee on Vaccine Safety (GACVS) is reviewing the data from Finland and Sweden regarding the increased risk of narcolepsy cases, especially in children and adolescents following the pandemic H1N1 vaccination (Pandemrix) in 2009⁽²⁹⁾. Although it is not a general worldwide phenomenon, but GACVS will continue to monitor the situation closely and we are waiting for future updates.

Low-Carbohydrate, Ketogenic Diet

Consuming a low-carbohydrate, ketogenic diet (LCKD) also known as Atkins diet, has some benefits for daytime sleepiness. It has been studied that narcoleptic patients show modest improvement in daytime sleepiness on LCKD⁽¹¹⁾. The goal behind LCKD is losing weight and maintaining body weight. Early studies showed that patients who have narcolepsy were more likely to be overweight and non-insulin-dependent diabetes⁽⁹⁾.

Avoid Low Vitamin D

Since narcolepsy with cataplexy is thought to be an immune –mediated disorder, it was proposed that vitamin D deficiency plays a role in autoimmune diseases. Further studies are needed to assess this proposal⁽³⁾.

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