Reducing the Clinical and Socioeconomic Burden of Narcolepsy by Earlier Diagnosis and Effective Treatment

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KEYWORDS

• Burden • Narcolepsy • Socioeconomic • Sleepiness • Cataplexy • Psychosocial • Comorbidities • Diagnosis

KEY POINTS

- Narcolepsy is a rare condition that carries a significant burden.
- The burden of narcolepsy is the result of clinical difficulties and disability directly related to the disorder and the socioeconomic liability.
- Time to appropriate diagnosis and treatment is generally prolonged and contributes to the burden.
- Effective treatment results in long-term benefits by improving clinical outcomes, potentially enabling improved education, increased employment opportunity, and improved work productivity and quality of life.
- Improved awareness about the diagnosis and tailored therapies improve clinical and socioeconomic outcomes by reducing time to effective treatment.

CLINICAL BURDEN

Age of Onset

The burden of narcolepsy varies with the age of onset. Although narcolepsy can begin at any age from infancy to the 80s or older, there is generally a bimodal distribution of symptom onset with an initial main peak at 15 years old and a lesser second peak at approximately 35 years old.[1,2] An analysis of 1000 patients with narcolepsy of all ages showed a median onset at 16 years and a median age of diagnosis of 33 years,[3] consistent with the known epidemiology and also suggesting the additional challenge of delay in diagnosis.

When narcolepsy begins in childhood, not only are the symptoms more difficult to recognize but the disorder is often misdiagnosed. In addition, even when appropriately identified, many of the medications prescribed for the treatment of narcolepsy are not approved for use in the pediatric population. Therefore, treatment is often delayed and less effective, commonly resulting in compromised learning and impaired education, as well as the development of psychosocial difficulties.[4] Similarly, consequences seen in the working age group (18–65 years old) can include impairment that may lead to loss of employment with frequent job changes, and, in the elderly (>65 years old), retirement may be earlier than desired and postretirement activities may be curtailed and adversely affected because of symptoms.

Symptom Evolution and Effects

The 5 main symptoms of narcolepsy are sleepiness, cataplexy, hypnagogic hallucinations, sleep paralysis, and disturbed nocturnal sleep.

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Cataplexy, the pathognomonic symptom of narcolepsy, is the abrupt loss of muscle tone provoked by a strong emotion. Cataplexy in adults is mainly precipitated by positive emotions such as laughter, elation, or happiness, although it can be precipitated by negative emotions such as anger. When obvious, such as when a person laughs and falls to the ground, cataplexy often leads to a rapid diagnosis of narcolepsy. However, most patients do not have falls associated with cataplexy; instead, they have more subtle symptoms such as facial, head, or limb weakness, which may be more difficult to diagnose. Cataplexy can be misdiagnosed as a drop attack, seizure, or a psychogenic symptom.

In children, the triggers and symptoms of cataplexy can differ from adults; precipitating factors can include exhaustion, tiredness, and stress, and symptoms can be described as the child having puppetlike movements.[5] However, symptoms usually evolve into the more typical form of cataplexy as the child ages.[6] Patients describe knee buckling that may lead to falls, but sometimes cataplexy may be only an abnormal sensation felt in the muscles with emotion. Other features of cataplexy may be facial weakness, with the inability to smile or drooping of the eyelids or head, and facial twitching or grimacing. In addition, objects may be dropped from the hands, or stumbling or incoordination can cause falls.

Sleepiness is not only the most common feature of narcolepsy but also generally the most disabling. In children, the initial presentation of abnormal sleepiness can be increased total sleep during the 24-hour day.[6] The sleepiness of narcolepsy is an unrelenting persistent symptom that can have fluctuations in severity but is always present. Typically, it is most evident when the patient is sedentary or inactive, such as when watching television, reading, sitting quietly, or when a passenger in a car. However, patients can also experience a momentary sleep, in which they can continue wakeful activities, such as driving, but memory formation may be impaired, thereby leading to automatic behavior episodes, behaviors for which the patient has no memory. The patient is capable of acting appropriately, but has no recall for the activity.

Vivid dreams at sleep onset are a common feature and often occur before falling asleep, leading to hypnagogic hallucinations, which are usually visual but can be auditory. Dreams on awakening (hypnopompic dreams) also occur, but are less specific to narcolepsy. Frequent dreams, nightmares, and lucid dreams are common.[7,8] Delusional dreams, in which the patient after awakening believes the activity really occurred, are more common than hypnopompic dreams in narcolepsy.[9]

Patients with narcolepsy have disturbed nocturnal sleep, which is characterized by sleep fragmentation, increased lighter sleep, and reduced deep sleep.[10] There are frequent fragmented, brief, nightly awakenings with difficulty returning to sleep and overall poor sleep quality. The sleep disturbance may be a major concern of the patient and often requires specific treatment.

In addition, patients with narcolepsy have abnormalities of rapid eye movement (REM) sleep and REM sleep motor regulation.[11] For example, sleep paralysis is a partial manifestation of REM sleep leading to an inability to move for seconds or minutes and can occur in the transition from sleep to wakefulness or from wakefulness to sleep, often in association with dreams or hallucinations. However, sleep paralysis occurs frequently in healthy individuals and so may not raise a suspicion of narcolepsy. In contrast, REM sleep behavior, which is dream-driven activity that occurs while asleep,[10] is a pathologic feature that can manifest as a part of disrupted REM sleep and can also be a cause of bodily injury to the patient and potentially the bed partner.

Cognitive Deficits

Patients with narcolepsy frequently complain of memory difficulties, trouble with attention, and deterioration of executive function. Memory problems are among the most frequent complaints in patients with narcolepsy. Complaints include forgetfulness and problems in following conversations.[12] However, it is possible that the disturbed sleep patterns in narcolepsy, rather than daytime sleepiness, are responsible for impaired memory.[13] Attention is affected on tasks that require an extended period of time or that require the ability to focus, or divided attention. In simple tasks narcoleptic patients seem to be able to compensate for arousal fluctuations by increases in alertness for short periods of time. More demanding tasks require the need to use effort to keep high arousal levels but this leads to speed-accuracy trade-offs, with patients performing less accurately or more slowly.

Executive function impairments are caused by attentional and cognitive resources that have to be allocated to the continuous maintenance of alertness, with the result that tasks are not performed quickly or accurately. Decision making is also affected in narcoleptics with a tendency toward risky choices possibly caused by changes in reward processing associated with reduced hypocretin levels.[14–17]