Assessment and management of excessive daytime sleepiness

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Daytime sleepiness affects 10% of the middle-aged but is often missed because clinicians fail to ask the appropriate questions, thus depriving patients of large potential treatment benefits. A sleep history must be taken as routinely as a cardiac, neurological or other system history.

Background

Obstructive sleep apnoea/hypopnoea syndrome

The obstructive sleep apnoea/hypopnoea syndrome (OSAHS) is much the commonest 'medical' cause of sleepiness (Table 1), occurring in 1–4% of the middle-aged. OSAHS is the combination of sleepiness or two other major symptoms, such as unrefreshing sleep, difficulty concentrating and nocturnal choking, with five or more apnoeas plus hypopnoeas per hour slept ('apnoea' is defined as a 10-sec pause in breathing, 'hypopnoea' as a 10-sec period during which ventilation is reduced by 50%). OSAHS results from pharyngeal narrowing due to jaw structure or obesity (although only 50% sufferers are obese). It causes a threefold risk of road accidents[1] and raises blood pressure independent of confounders.[2,3]

Table 1. Causes of sleepiness in approximate order of frequency.

- Insufficient sleep
- Shift working
- Obstructive sleep apnoea/hypopnoea syndrome
- Psychological or psychiatric illness, especially depression
- Sedative or stimulant drugs
- Narcolepsy
- Idiopathic hypersomnia
- Central nervous system hypersomnia
- Menstrual-related hypersomnia
- Kleine-Levin syndrome

Narcolepsy

Narcolepsy is 100 times less common than OSAHS, occurring in 0.04% of the population. The symptoms of sleepiness and cataplexy (Table 2) usually develop in teenage or early adult life. Sleep paralysis, hypnagogic hallucinations and fragmented nocturnal sleep are common but non-specific features. Narcolepsy is associated with decreased hypothalamic production of hypocretin.[4] The association of narcolepsy with HLA DQB1*0602 and the absence of symptoms in childhood suggest that the hypocretin deficiency is acquired, perhaps due to an autoimmune response.[5]

History

Before the initial consultation, sleepy patients and their partners should complete sleep questionnaires (Table 3). The responses usually allow the physician to start the consultation with a probable diagnosis. The three commonest medical causes of sleepiness can usually be differentiated on history alone (Table 4). In practice, I define significant sleepiness as an Epworth Sleepiness Scale (ESS) score above 11 (Table 5) or recurrent problems with sleepiness whilst driving or actively working.

Investigations

Most sleepy patients require further investigation, the exceptions being those with clearly inadequate sleep duration (<6.5 hours per night) or shift workers, but some of these may require investigation if the sleepiness is troublesome and they have symptoms of OSAHS.

There is considerable dispute about the type of overnight investigation required. The traditional approach was polysomnography (Table 6), recording up to 30 neurophysiological and respiratory signals overnight, but there is no evidence that this is needed to diagnose OSAHS or narcolepsy.[6,7] UK waiting times for investigation and treatment of patients with possible OSAHS extend up to five years.[8] This is one reason for using limited sleep studies, with recording of respiratory pattern and oximetry[9] as a quicker, cheaper alternative to polysomnography with similar clinical outcomes. We perform limited studies at home as our diagnostic study, using polysomnography only in those with severe sleepiness and an equivocal home study.

Routine daytime testing of sleepiness is unnecessary in OSAHS. However, in professional drivers and other drivers who remain sleepy on treatment, daytime tests of ability to stay awake, either the Maintenance of Wakefulness Test or Osler Test,[7] have some face-validity; those unable to stay awake during a day of high stakes assessment are unlikely to stay awake driving on motorways[10] – but the converse is not true.

Narcolepsy has neither specific features on overnight recording nor a specific diagnostic test. The most watertight diagnostic criteria are histories of sleepiness and cataplexy associated with a mean

Table 2. The symptoms of narcolepsy.

Principal symptoms	*Excessive daytime sleepiness* with recurrent naps *Cataplexy*: episodes of partial or total loss of muscle tone in response to emotion, especially on laughter, usually lasting <1 min
Associated, but non-specific, symptoms (not required for diagnosis)	*Sleep paralysis*: episodes of inability to move on awakening, often frightening, sometimes accompanied by dream mentation *Hypnagogic hallucinations*: dream-like imagery occurring at sleep onset *Fragmented sleep*: people with narcolepsy typically have disturbed nocturnal sleep

sleep latency of less than eight minutes, and rapid eye movement (REM) sleep within 15 minutes of sleep onset on two of the five naps on a Multiple Sleep Latency Test (MSLT). Repeat MSLTs can be helpful. HLA typing is not diagnostically useful.

In patients with possible narcolepsy without cataplexy, the diagnostic criteria should be more strict. Thus, we perform polysomnography on these patients to exclude OSAHS, followed by an MSLT. Those with normal polysomnography and a mean sleep latency of less than eight minutes with two sleep onsets with REM (SOREM) – and no other reasons for SOREMs such as sleep deprivation, OSAHS or drug withdrawal – can be diagnosed as having 'narcolepsy without cataplexy'.

Table 3. Topics in sleep questionnaire for sleepy patients.

Sleep duration and quality	• Normal bed or lights out time on working days and weekends • Usual time to fall asleep • Time of final awakening working days and weekends • Number and duration of wakenings throughout the night • Cause of nocturnal wakening
Daytime naps, frequency, situation and duration	• Shift working • Precise timing and pattern of shifts
Duration of symptoms	• Age at onset • Progression of symptoms • Severity of symptoms
Associated symptoms	• Snoring, including frequency, severity and positionality • Witnessed apnoeas • Nocturnal choking • Unrefreshing sleep • Cataplexy • Hypnagogic hallucinations • Sleep paralysis • Witnessed recurrent limb movements during sleep
Predisposing factors	• Weight gain • Quantity of alcohol consumed • Family history of sleep apnoea or narcolepsy • Psychological or psychiatric illness • Potentially sedating or stimulant drugs, including caffeine
Severity of sleepiness	• Epworth or other sleepiness scale • Frequency and consequences of sleepiness: – driving – at work – in embarrassing social situations • Effect on work performance and ability to concentrate

Table 4. Clinical pointers in sleepy patients.

	OSAHS	Narcolepsy	IHS
Age of onset (years)	35–60	10–30	10–30
Night sleep:			
Duration	Normal	Normal	Long
Awakenings	Occasional	Frequent	Rare
Snoring	Yes	Occasional	Occasional
Apnoeas	Yes	Occasional	Occasional
Morning drunkenness	Occasional	Occasional	Common
Day symptoms			
Cataplexy	No	Yes	No
Day naps			
Frequency	Usually few	Many	Few
Time of day	Afternoon/evening	Afternoon/evening	Morning
Duration	<1 hour	<1 hour	>1 hour

IHS = idiopathic hypersomnia; OSAHS = obstructive sleep apnoea/hypopnoea syndrome.

Management

Management will differ according to cause but all sleepy individuals must be told the risks of driving when sleepy.[10] Around 20% of accidents on major roads are caused by sleeping drivers, the risks being highest at 2–6 am and 2–4 pm. The Driver and Vehicle Licensing Authority (DVLA) has recently produced a useful publication clearly putting the onus on the sleepy driver to be safe and report relevant medical causes.[11]

Insufficient sleep

Sleep restriction causes sleepiness, irritability, depression and impaired concentration. If sleep deprivation is work related, much longer sleep durations at the weekend are common and can be diagnostically helpful. Management is by education about the hazards of sleepiness, combined with encouragement to increase sleep time by an hour or more each night.

Table 5. Epworth Sleepiness Scale.

Patients are asked to rate their sleepiness levels in normal daytime situations and to grade from 0–3 their likelihood of dozing/falling asleep, in contrast to just feeling tired:
0 = would never doze
1 = slight chance of dozing
2 = moderate chance of dozing
3 = high chance of dozing

Situations:
- Sitting and reading
- Watching TV
- Sitting inactive in a public place; for example, a theatre or meeting
- As a passenger in a car for an hour without a break
- Lying down to rest in the afternoon
- Sitting and talking to someone
- Sitting quietly after lunch (without alcohol)
- In a car, while stopped in traffic

Shift work

Problems are most common in those on rotating shifts. Workers on permanent night shifts who revert to nocturnal sleep patterns on their nights off – as most do – may also have major problems. Older people have greater difficulty adjusting to shifts;[12] those aged over 45 years should be given the option of daytime working when possible. Shift work is associated with an increase in road accidents. Rotating shifts should be designed to have long cycle lengths with at least a week on each shift, and shifts should be progressively delayed when changed, thus moving from morning shift, to late shift, to night.[7]

Obstructive sleep apnoea/hypopnoea syndrome

Weight loss and evening alcohol avoidance should be recommended for those with OSAHS. Continuous positive airway pressure (CPAP) by nasal or face mask is the first-line therapy for OSAHS. There is robust evidence[9] that CPAP improves symptoms, sleepiness, health status, cognition, mood, driving ability and blood pressure in OSAHS. CPAP reduces mean diastolic blood pressure by about 4–5 mmHg in patients with 20 or more 4% desaturations per hour.[2,3] CPAP is effective but obtrusive, and patients require considerable education and support to adopt CPAP successfully. Over 98% of patients for whom we recommend CPAP start treatment successfully. Long-term use is increased by intensive nurse-led support.[13]

Key Points

A sleep history should be taken routinely

Anyone with recurrent sleepiness when driving or a score above 11 on the Epworth Sleepiness Scale, despite adequate nocturnal sleep duration, needs investigation

There is robust evidence that treatment of the obstructive sleep apnoea/hypopnoea syndrome improves clinical features including blood pressure

Continuous positive airway pressure is the treatment of choice, with mandibular repositioning splints as second-line therapy

Narcolepsy is characterised by sleepiness plus cataplexy and is caused by hypocretin deficiency

KEY WORDS: hypersomnia, narcolepsy, obstructive sleep apnoea/hypopnoea syndrome, shift work

Sleepy patients with frequent apnoeas/hypopnoeas use CPAP well: over 90% of those with more than 30 apnoeas plus hypopnoeas per hour and an ESS score of 11 or higher are using CPAP regularly at three years[14] – comparing well with drug use in other chronic conditions. However, long-term use of CPAP is poorer in patients with 5–15 apnoeas per hour despite short-term benefit from the procedure.[7] Recent advances in CPAP include the development of intelligent devices which deliver varying pressure and may improve outcomes.[15] Patients complying with CPAP who deny sleepiness are usually allowed by the DVLA to drive cars.

Mandibular repositioning splints (MRS), which hold the mandible forward, thus enlarging the upper airway, can improve sleepiness, symptoms and blood pressure in OSAHS.[16] Comparative trials indicate that CPAP remains the treatment of choice with greater efficacy,[17,18] but MRSs are good second-line therapy. There is little or no role for stimulants in OSAHS and none for uvulopalatopharyngoplasty.

Table 6. Sleep laboratory investigations.

Polysomnography	Assesses overnight brain activity, muscle tone, eye movements, chest and abdominal movements related to breathing, oral or nasal airflow, heart rate and oxygenation
Multiple Sleep Latency Test (MSLT)	Quantifies daytime sleepiness by offering 4–5 opportunities when the subject is asked to try to fall asleep during the day at 2-hour intervals Sleep latency and REM sleep latency defined by EEG, eye movements and muscle tone
Maintenance of Wakefulness Test (MWT)	As in the MSLT, the subject is given repeated opportunities of quiet, but asked to try to stay awake Latency to sleep, if it occurs, is measured by EEG

Patients taking sedative or stimulant drugs

Sleepy patients on sedative or stimulant drugs should gradually withdraw them to see whether this helps.

Narcolepsy

Until effective hypocretin analogues become available, therapy will remain based on improving sleep hygiene, encouraging planned daytime naps and drug therapy. The principal drugs used for sleepiness are modafinil and amphetamines.

Modafinil

Modafinil is a non-amphetamine effective in narcolepsy,[19] but there are no data directly comparing modafinil with other drugs. It is expensive and has no anticataplectic effect but, because of proven efficacy, few side effects and low abuse potential, modafinil is the first-choice agent.[20]

Amphetamines

Amphetamines have greater effect on sleepiness, improving sleepiness in over

90% of patients and cataplexy in most, but they produce side effects which are often limiting. The usual doses of methylphenidate and dexamphetamine are 10–60 mg/day and 5–60 mg/day, respectively,[7] starting at the lowest dose and building up as required. Drug holidays can be useful when tolerance develops.

Cataplexy

Cataplexy is caused by the REM sleep-related phenomenon of postural hypotonia intruding into wakefulness and is treated by suppressing REM with antidepressants. My practice is to start with fluoxetine 20–60 mg/day or clomipramine 25–200 mg/day.

Uncommon syndromes

Idiopathic hypersomnia

Idiopathic hypersomnia is a very rare, poorly characterised condition in which patients have prolonged sleep durations, are difficult to waken in the morning and may have automatic behaviour in association with microsleep intrusion into wakefulness. Its diagnosis is one of exclusion, with no positive diagnostic test; it requires evidence of objective daytime sleepiness, preferably on an MSLT where the absence of sleep onset REM is helpful to differentiate from non-cataplectic narcolepsy. Stimulants can help, but modification of lifestyle and sleep habits and planned daytime naps produce little benefit.

Central nervous system hypersomnia

This rare condition can occur following head injuries, cerebrovascular disease and encephalitis. Stimulants can help.

Menstrual-related hypersomnia

Another rare condition for which oral contraceptives may be of benefit is menstrual-related hypersomnia.

The Kleine-Levin syndrome

The rare Kleine-Levin syndrome is characterised by recurrent attacks of sleep, often for more than 20 of the 24 hours for several days. It is associated with bizarre eating and sometimes hypersexuality,[7] starts in teenage life and is more common in males. Stimulants and lithium may also reduce attacks in some, but not all, patients.

Conclusions

Sleepiness is common and dangerous but often overlooked by doctors. Appropriate diagnosis and treatment can greatly improve the quality of life and work performance of affected individuals, road safety for the sufferer and others, and decreased cardiovascular risk in OSAHS.

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Further reading

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