Case Report

The Challenge of Excessive Daytime Sleepiness

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Abstract

Excessive Daytime Sleepiness (EDS) is a common symptom in patients with insufficient and disrupted sleep, or a manifestation of underlying depression. Diagnosing sleep-disordered breathing by nocturnal polysomnography (PSG) and commencing positive pressure ventilation can effectively control the breathing abnormality and improve sleep. However, EDS often persists in some patients. We present a challenging case of severe central sleep apnea (CSA) with EDS.

A 25-year-old female Nursing student with an Epworth Sleepiness Score (ESS) of 20/24 was referred for investigation of suspected narcolepsy. She was a part-time shift-worker with history of intravenous (IV) drug abuse (on a Methadone Maintenance program), depression and restless legs syndrome. The PSG showed severe CSA with an Apnea Hypopnea Index (AHI) of 74/hr. The Multiple Sleep Latency Test (MSLT) showed a very short sleep latency of <1 minute. The urine drug screen was positive for opioids and Methadone.

Patient was commenced on treatment with Adaptive Servo Ventilation (ASV) and her AHI improved to 11/hr. However, the ESS declined only marginally from 20/24 to 18/24. Effective treatment of sleep breathing disorder did not resolve EDS, which was associated with other factors.

ABBREVIATIONS

EDS: Excessive Daytime Sleepiness; PSG: Polysomnography; CSA: Central Sleep Apnea; ESS: Epworth Sleepiness Score; MSLT: Multiple Sleep Latency Test; AHI: Apnea Hypopnea Index; ASV: Adaptive Servo Ventilation; SOREMS: Sleep Onset Rapid Eye Movement Sleep; CPAP: Continuous Positive Airway Pressure.

INTRODUCTION

Excessive Daytime Sleepiness (EDS) is often debilitating for patients and may have multiple contributing factors. Narcotic-induced central sleep apnea (CSA) is common in patients on narcotic replacement therapy and it’s severity is dose-dependent. Adaptive Servo Ventilation (ASV) can stabilize breathing patterns in affected individuals. However, effective treatment of CSA may not eliminate EDS, which may be multi-factorial.

CASE PRESENTATION

A 25-year-old nursing student presented to the sleep clinic with severe EDS for several years. She never felt rested and could fall asleep anywhere, anytime. She could not concentrate during her nursing education classes and was falling asleep during intercourse with her partner. She dozed off while driving on five separate occasions and had one motor vehicle accident sustaining minor injury. Her Epworth Sleepiness Scale (ESS) score was high at 20/24. The patient described vivid dreams resembling hypnogogic hallucinations, incidents of sleep paralysis and violent leg movements during sleep.

The patient had a history of depression with one prior hospital admission after an attempted suicide. She admitted IV drug abuse and claimed to have abstained from hero in for over 8 months. She was on methadone maintenance treatment for the same period and worked multiple casual shifts at a transport call centre and pharmacy.

Her regular medications include: Citalopram 40 mg daily, Methadone 85mg daily, an oral contraceptive pill, fish oil capsules and calcium tablets.

Examination revealed a fit young woman with a height of 156 cm, weight of 60 kg and BMI 24.7 kg/m². Mild crowding of the oropharynx was noted (modified Mallampati score -2). Cardiovascular, respiratory, abdominal and neurological examinations were normal, with no evidence of peripheral neuropathy.

An overnight polysomnography (PSG) was performed at the hospital sleep laboratory using Philips Respironics Alice LE™ sleep recording system. Scoring criteria were compliant with the American Academy of Sleep Medicine task-force manual [1] and commentary on the above manual by Australasian Sleep Technologists Association / Australasian Sleep Association [2]. PSG showed severe, predominantly central sleep apnea (Figure

1) with an apnea-hypopnea index (AHI) of 74/hr. There was Periodic Limb Movements of Sleep (PLMS) of mild severity and uncertain clinical significance.

Multiple Sleep Latency Test (MSLT) [3,4] (Table 1) followed the PSG as per protocol and showed shortened sleep latency (average sleep latency [4 values] of 0.125 minutes); confirming EDS. There was no sleep onset REM sleep (SOREMs) detected.

Her HLA-DRB1 was 01:02.13:01 and HLA-DQB1 - 05:01.06:03 subtype, usually not associated with narcolepsy. The urine drug screen was positive for narcotic opiate > 300μg/L (includes morphine, codeine, nalorphine and heroin including its metabolite, 6-monoacetylmorphine) and methadone/metabolite > 100μg/L suggesting recent abuse of heroin.

Confronted with the positive urine drug screen report, the patient reluctantly confessed abusing heroin just a few days prior to her appointment. She was encouraged to invite her concerned mother into the consulting room and explain the findings to her, which had a major impact on her further treatment adherence.

Negative urine drug screens on subsequent visits confirmed that the patient stopped abusing heroin for at least 12 months follow-up.

Goldberg’s Depression Scale [5] was used to monitor her depression while on anti-depressant treatment. She was encouraged to take short daytime naps to help cope with EDS. She gave up her shift-work to concentrate on her studies.

For her predominantly central sleep apnea she was commenced on Adaptive Servo Ventilation (ASV). The Auto-ASV titration study showed 90% of the time device pressure support required was 10 cmH2O. Therefore, she was commenced on 10cm H2O pressure support ASV as per accepted practice with dramatic AHI reduction from 74/hr to 11/hr. Initial downloads from the machine showed poor compliance with treatment, with an average daily use of 1 hour 48 minutes. Regular review and encouragement improved her daily ASV compliance to 5 hours 9 minutes.

EDS, however, remained with modest ESS decline from 20/24 to only 18/24, indicating other contributing factors. Her symptoms of restless legs also improved with treatment of CSA. She had lost her driving license due to her multiple driving misadventures and was referred by driving authorities for further assessment of her fitness to drive.

**DISCUSSION**

Excessive day time somnolence (EDS) is the commonest reason for referral to sleep clinic [6]. The prevalence of EDS is high in adolescents, shift-workers and the elderly [7]. Differential diagnosis of EDS is diverse and includes sleep-breathing disorders, psychiatric disorders; movements disorders (e.g. periodic limb movement disorder, REM sleep behavior disorders, somnambulism) or sleep deprivation (e.g. shift-work, chronic medical conditions, drug or substance abuse). In our patient multiple factors contributing to EDS were identified.
Abbreviations:

- MINS: minutes
- REM: Rapid Eye Movement

### A) Central sleep apnea

Severe CSA (AHI = 74/hr) was fragmenting the patient’s sleep and caused by chronic opioid abuse. Opioid use, both acute and chronic, has been associated with sleep-disordered breathing [8,9]. Several studies have shown a marked increase in sleep-disordered breathing with both acute and chronic use of narcotics, regardless of the agent used, dose, duration of therapy, or individual risk factors [9-15].

The type of sleep-disordered breathing associated with chronic opioid use is controversial. CSA has traditionally been thought to be the predominant form of sleep apnea in patients with opioid dependence. However, more recent reports have shown that Obstructive Sleep Apnea (OSA) is more common in patients on opioid therapy [14,16]. With regards to sleep-disordered breathing the Methadone maintenance cohort is distinct from the patients treated with opioids for chronic pain having a lower incidence of obstructive events. One possible explanation for this difference is the difference in body mass index between these populations and that pain itself affects sleep quality. Concomitant medications (e.g. benzodiazepines & antidepressants) could compound the action of opiates on the Central Nervous System.

In a study assessing methadone maintenance treatment patients who complained of EDS, OSA was more common than CSA (16) 35%-57% of patients managed in long-term pain clinic were detected to have OSA [17].In our patient PSG showed mainly central events (64/74), (7/74) were mixed events, while only 0.4/74 were obstructive. The intuitive treatment for opioid-induced sleep-disordered breathing is withdrawal or at least reduction of the opioid dose. Improvement, or even resolution, of sleep-disordered breathing after cessation of medication has been reported in one patient [17]. However, this is rarely feasible in most clinical scenarios, at least in the short-term.

Under these circumstances positive airway pressure (PAP) treatment is the most effective treatment option. Patients with opioid-induced sleep apneas seem more refractory to treatment with positive airway pressure therapy. The CSA often requires bi-level positive airway pressure (BiPAP) ventilation or adaptive servo ventilation (ASV). An ASV device is able to treat central sleep apnea by providing variable pressure support. They provide positive airway pressure during expiration to eliminate obstructive events and back-up mandatory breaths to treat central apneas. In our patient, we prescribed ASV without an initial trial of CPAP due to the finding of predominantly central events on PSG. This decision is supported by recent study by Javaheri et al [18],Guilleminault et al [19] conducted laboratory based titration study with both CPAP and BiPAP and found residual CSA in most of his patients. In another study, Farney et al [20] examined the result of one overnight use of each CPAP, BiPAP with back-up ventilation and ASV on a small cohort of patients on long-term opioids. Both BiPAP with back-up ventilation and ASV showed better resolution of apneic episodes compared to CPAP alone [20]. Similar to other forms of CSA, both BiPAP and ASV are more effective in controlling respiratory events and normalizing objective sleep measures compared to CPAP. However, no studies have compared long-term outcomes among these different treatment options.

### B) Sleep Hygiene and Shift Work

Our patient was a part-time shift worker as well as a nursing student. The international classification of sleep disorders (ICSD) 2nd edition (1) diagnostic criteria for Shift Worker Disorder (SWD) requires that other current sleep disorder needs to be excluded before a diagnosis of shift work disorder can be made. However, following treatment of CSA with ASV, we believe, shift-work was impacting on the circadian rhythm of our patient and affecting her sleep quality.

### C) Restless Legs Syndrome

Our patient had a history of restless legs, which only partially fulfilled the clinical diagnostic criteria prescribed by the International (RLS) study group [21]. RLS is roughly twice as prevalent in females as males and prevalence increases with age up to age 64 [22]. However, there are very few studies on the occurrence of RLS in females under the age of 40 years apart from studies in pregnant women [23]. Symptoms suggestive of restless legs in our patient improved with ASV treatment.

### D) Depression

Our patient had a history of treated depression. EDS is a very common symptom of depression and occurs in up to 80% of depressed patients [24]. It is interesting that following response to treatment, if EDS persists it can frequently predict recurrence of new episode of depression or relapse [25] and may be a meaningful clinical marker of undertreated depression [26]. However, the Goldberg Depression Scale did not confirm ongoing depression in our patient.

### E) Methadone and EDS

Patients on methadone maintenance therapy for opioid dependence complain about EDS frequently [28,29]. This seems to correlate with years of opiate abuse before commencing on a Methadone maintenance program and also with the methadone

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**Table 1:** MSLT (Multiple Sleep Latency Test) Patient given 4 nap times 2 hours apart.

<table>
<thead>
<tr>
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<th>Nap Test 1</th>
<th>Nap Test 2</th>
<th>Nap Test 3</th>
<th>Nap Test 4</th>
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<td>13.5 mins</td>
<td>15 mins</td>
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<tr>
<td>Sleep latency</td>
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<td>0.5 mins</td>
<td>&lt;0.5 mins</td>
<td>&lt;0.5 mins</td>
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<tr>
<td>REM latency</td>
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**Abbreviations:** MINS: minutes; REM: Rapid Eye Movement
dose required to control symptoms [29]. However, a more recent study [27] did not find the dose of Methadone to be associated with disturbed sleep. Our patient was on a moderate-dose methadone and its impact on her EDS is uncertain.

CONCLUSION

In our young patient with opioid-related severe CSA, ASV was effective in controlling central apneas, but failed to resolve the EDS. We argue that a combination of lack of sleep due to shift work, and studying, contributed to behavior-induced insufficient sleep. Continued opioid use was an additional contributor for persistent EDS.

REFERENCES

5. NSF. Determinants and measurements of daytime sleepiness. Primary Care Sleep Medicine: A Practical Guide. 2007:61-82.

Cite this article