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Research Article

The Assessment of Hypersomnolence: A Clinical Experience

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Abstract

Introduction: Excessive Daytime Somnolence (EDS) is a common complaint amongst patients presenting to a Sleep Clinic. Sleep deprivation is a major cause of EDS and therefore its accurate assessment is essential.

Methods: All patients referred for a Diagnostic Sleep Study (DSS) and Multiple Sleep Latency Test (MSLT) for the investigation of EDS were invited to participate in the study. Patients wore an actigraph armband and completed a sleep diary for at least 7 days. Patients had blood tests excluding medical reasons for fatigue and completed questionnaires: Functional Outcome of Sleep Questionnaire, Depression Anxiety Stress Scales and Short Form Fatigue Questionnaire.

Results: 64 patients were referred for the investigation of EDS during the study period; 33 patients were unsuitable due to co-morbidities, 4 declined and 27 consented. 3 patients were further excluded because of co-morbidities not known at time of consent. 7/24 patients were excluded due to the presence of obstructive sleep apnoea and/or iron deficiency, or reduced total sleep time (<300minutes) on polysomnography. 10/17 patients had a Mean Sleep Latency < 8minutes. 1/10 patients who slept more 7hours per night (on actigraphy) with a Mean Sleep Latency of 5.8minutes could be labelled with Idiopathic hypersomnolence, using ICSD-3 criteria.

Conclusion: The use of actigraphy, blood work up, and questionnaires provides a more accurate assessment of EDS, as it allows the exclusion of patients with a possible medical and/or psychiatric etiology for fatigue and/or those patients who are sleep deprived.

Keywords: Excessive daytime somnolence; Polysomnography; MSLT; Actigraphy; Sleep diary

Abbreviations

EDS: Excessive Daytime Somnolence; TST: Total Sleep Time; DSS: Diagnostic Sleep Study; MSLT: Multiple Sleep Latency Test; RDI: Respiratory Disturbance Index; PLMS: Periodic Leg Movements; PSG: Polysomnography; EEG: Electroencephalogram; EOG: Electro-Oculogram; EMG: Submental Electromyogram; ECG: 2-Lead Electrocardiogram; ASDA: American Sleep Disorders Association; DASS: Depression Anxiety Stress Scale; FOSQ: Functional Outcomes of Sleep Questionnaire; EUC: Electrolytes, Urea, Creatinine; LFT/CMP: Liver Function Test/Calcium, Magnesium, Phosphate; OSA: Obstructive Sleep Apnoea; BMI: Body Mass Index; SO: Sleep Onset; REM: Rapid Eye Movement; NREM: Non Rapid Eye Movement; MET: Metabolic Equivalent Task; AI: Arousal Index; CPAP: Continuous Positive Airway Pressure; IHS: Idiopathic Hypersomnolence.

Introduction

Excessive Daytime Somnolence (EDS) is a common complaint. There are many reasons for EDS: Primary sleep disorders, other medical conditions, drugs or chronic sleep deprivation. Medical conditions such as thyroid dysfunction, anaemia, depression and Vitamin D deficiency [1] have been be associated with daytime sleepiness and fatigue. These medical conditions can be easily accessed and managed clinically. The assessment and exclusion of sleep deprivation as a potential cause for EDS, however, can be more difficult in clinical practice as it is dependent on patient self reporting.

According to the National Sleep Foundation, 13% of American adults reported sleeping less than 6hrs per night in 2001 compared to 20% in the 2009 poll [2]. Sleep deprivation is known to be a major cause of sleepiness so its accurate assessment is very important. The sleep diary is a tool used for recording sleep/wake patterns in clinical practice providing subjective measurement of Total Sleep Time (TST). Tomita et al., 2013 [3] compared simultaneous sleep measurements using actigraphy and sleep diaries in patients being investigated for EDS. In this population, the results obtained using a sleep diary tended to estimate a statistically significant earlier sleep onset time and longer TST than those via actigraphy. 5 of the 24 (20.8%) patients reported >6hrs total sleep time on the sleep diary compared to <6hrs with a discrepancy of >1h. The results suggest that sleep deprivation can be missed when relying on patients sleep diary keeping only. Although it is common practice to ask patients to keep a sleep diary, an objective measurement of sleep time in conjunction with a sleep diary may be useful in patients complaining of excessive sleepiness [4]. An objective measurement of TST would definitively exclude sleep deprivation as a contributing factor to EDS.

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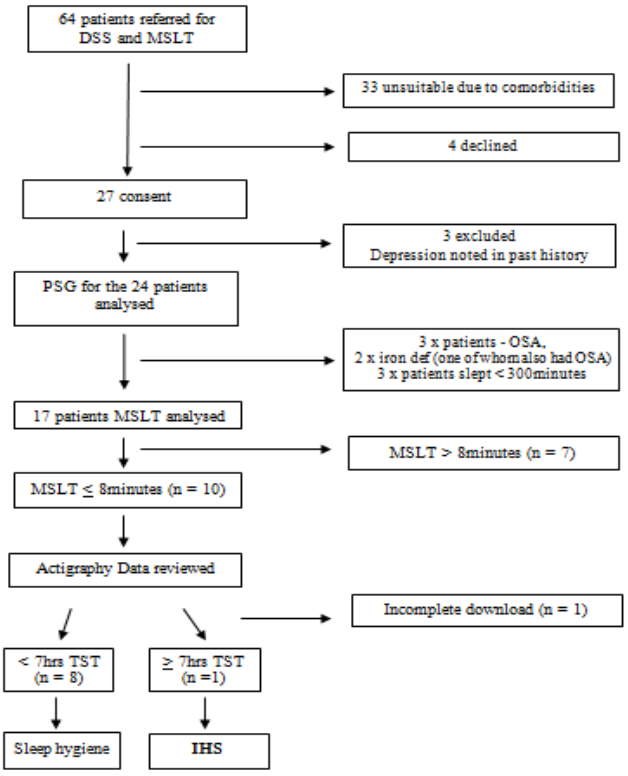

Figure 1: Diagnostic sleep study and MSLT.

Our objectives were to

1. Characterise a population referred to a clinical sleep laboratory for the investigation of excessive daytime somnolence, with strictly applied exclusions criteria as described by ICSD-2 [5].

2. Assess the usefulness of actigraphy in the assessment of EDS.

Methods

Subjects

Patients attending Concord Hospital Sleep Unit from April 2010 to December 2012 for a diagnostic sleep study (DSS) and Multiple Sleep Latency Test (MSLT) for the investigation of hypersomnolence were approached to participate in the study.

Our exclusion criteria were RDI > 15, minimum saturation < 88%, other primary sleep disorders (e.g. PLMS), patients with co-morbidities (anaemia, thyroid dysfunction, chronic pain, documented diagnosis of depression) which may result in sleep fragmentation and sleepiness and patients taking medications (antidepressants, analgesics, hypnotics) known to cause sleepiness and drowsiness.

Sensewear armband

Patients wore an actigraphy arm band (Body Media Sensewear™, Pittsburgh Pennsylvania) for up to 7 days. The armband was worn on the right arm with the dominant hand recorded on the device. The algorithm relies on a tri-directional movement sensor (x, y, z plane), body surface temperature, galvanic skin response and heat flux to determine sleep time versus awake. The data was downloaded and analysed using Sensewear software. Patients completed a sleep diary during the same period reporting 'time to bed', 'time out of bed' and wakefulness during the night.

Polysomnography

Standard Polysomnography (PSG) was performed using a computerised polysomnography system (Compumedics W-Series Sleep V2 sleep system, Melbourne Australia). The recording montage included electroencephalogram (EEG), Electrooculogram (EOG), Submental Electromyogram (submental EMG), 2-lead Electrocardiogram (ECG), effort of breathing (thoracic and abdominal RIP) and airflow (nasal prong pressure and oronasal thermistor). Overnight oximetry, leg movement accelerometer (anterior tibialis), sound and body position were also recorded continuously overnight. EEG (C3/A2, C4/A1, O2/A1) signals were monitored using gold cup electrodes (E5H, Grass, Canada) placed as per the International 10 20 system [6]. Sleep was staged according to the R & K rules [7]. Arousals were scored as per the ASDA criteria [8]. Obstructive apneas were defined as cessation of airflow for at least 10 seconds. Hypopneas were defined as a 50% reduction in nasal airflow from baseline for at least 10 seconds associated with a desaturation of at least 3% and/or an EEG arousal. All sleep studies were scored by trained sleep technologists.

Multiple Sleep Latency Test (MSLT)

For inclusion, patients needed to record more than 300minutes of sleep on PSG overnight preceding the MSLT. Patients were woken up at 6am, following the overnight sleep study, for an 8am MSLT start. 4-5 naps were performed using the 20-minute protocol [9]. Patients were instructed not to consume caffeine-based foods and drinks throughout the day. The first nap was commenced 2hours after the patient was woken up and then 2-hourly after that. The naps were conducted in a darkened, quiet room. Patients were asked to close their eyes, relax and allow themselves to fall asleep after lights out. Sleep onset was defined as the first epoch of any sleep stage. The patient was allowed to sleep for 15 minutes after sleep onset occurred. The nap was terminated after 20 minutes if no sleep onset occurred and a sleep latency of 20 minutes was used in the analysis. Patients were asked to get out of bed and maintain wakefulness until the next scheduled nap. Patients provided a morning urine sample for drug screen analysis.

Questionnaires

Patients completed the following questionnaires:

Depression Anxiety Stress Scale: The Depression Anxiety Stress Scale (DASS 21), a 21 item, self reporting questionnaire, measures symptom severity of depression, anxiety and stress. The patient scores the presence of a symptom over the previous week from 0 - 3. (0 = Did not apply to me, 1 = Applied to me to some degree or some of the time, 2 = Applied to me to a considerable degree or a good part of the time, 3 = Applied to me very much, or most of the time). DASS-21 is a shortened version of the original questionnaire (42 items) and as such the final score for each item needs to be multiplied by 2. Although the DASS score may contribute to the diagnosis of anxiety and depression, it is not a diagnostic tool. The higher the DASS score the higher the level of distress [10].

Functional Outcomes of Sleep Questionnaire (FOSQ): The

Functional Outcomes of Sleep Questionnaire (FOSQ) measures the impact of daytime sleepiness on activities of daily living. The patient is required to complete 30 questions. The potential range of scores is 5-20. The higher the score the lower the impact on the patient [11].

Fatigue Score: The short form fatigue questionnaire is used to assess a 'sense of tiredness, lack of energy or total body give-out". The patients are required to rate 9 statements (with respect to the last 2 weeks) from a score of 1 – 7 (1 = completely disagrees with the statement and 7 = completely agrees with the statement). A lower score equates to less fatigue experienced by the subject [12].

Blood tests: All patients underwent a Full Blood Count, EUC, LFT/CMP, Thyroid function studies and 25 Hydroxy – Vitamin D testing designed to assist in excluding any medical reasons for fatigue.

Statistical analysis

Mean and standard deviations reported. A non parametric comparison of means for independent samples using Wilcoxen ranked sums was performed, to determine differences between those with MSL<8 (idiopathic hypersomnia) and those with MSL>8 minutes. A p value <0.05 was considered significant.

This study was approved by the Concord Hospital Ethics Committee.

Results

Sixty four (32F) were referred for a diagnostic sleep study and MSLT for the investigation of excessive daytime sleepiness (Figure 1).

33 patients were found to be not suitable for recruitment due to known OSA, other medical conditions such as the presence of chronic pain and use of medications which can contribute to daytime sleepiness. 4 patients declined to participate. 27 patients were consented; of which 3 were further excluded (2 patients were found to have clinical depression in the clinical history, 1 patient with a recent change in medication (Thyroxine) just prior the sleep study).

Of the 24 patients, 3 were found to have OSA (RDI; 16.4, 23.5, 12.6) on PSG. The patient with an RDI of 12.6/hr was excluded due to significant desaturation. 2 patients (one of whom had OSA) were iron deficient, 3 slept less than 300minutes on PSG. Demographic and polysomnographic data for the remaining 17 patients selected for analysis is shown in (Table 1).

The 17 patients had a mean age of 35 + 12 years and a BMI of 26.7 + 5.8 kg/m^2. Mean total sleep time was 368.0 + 48.0 minutes and mean sleep efficiency 82.0% + 10.0%

Sleep Onset (SO) was within normal range occurring 27 + 35 minutes after 'lights out' and REM sleep onset 108 + 52minutes. Sleep architecture was also within normal range with NREM as a % of TST 82.4 + 4.0 and REM as a % of TST 17.6 + 4.0.

Sleep apnoea and sleep fragmentation was excluded with a mean RDI of 3.3 + 3.8/hr of sleep and mean AI of 8.1 + 5.2/hr of sleep. Mean sleep latency for the group was 8.8 + 4.1 minutes. Mean TST as recorded on actigraphy was 368 + 54.8minutes compared to 458.0 + 86.0 minutes reported on the patient's sleep diary.

1 Metabolic Equivalent Task (MET) is defined as the amount of oxygen consumed while sitting at rest and is equal to 3.5ml O_2 per kg body weight x minutes. The mean METS, as recorded by the Sensewear armband, was 1.5 + 0.28.

Table 1: Demographic and Polysomnographic data.

	Mean±SD
n = 17 (8 F)	
Age (yr)	39±12
BMI (kg/m^2)	26.7±5.8
Mean Total Sleep Time (min)	368±48
Mean Sleep Efficiency (%)	82±10
Respiratory Disturbance Index (RDI/ hr sleep)	3.3±3.8
Arousal Index (AI/hr)	8.1±5.2
Sleep Onset (min)	27±35
REM Sleep Onset (min)	108±52
Mean Sleep Latency - (min)	8.8±4.1
Mean TST - Actigraphy (min)	368±54.8
Mean TST - Sleep Diary (min)	458±86
Mean Mets (3.5 ml $O_2 \cdot kg^{-1} \cdot min^{-1}$)	1.5±0.28

Table 2: Blood test results for the 17 patients.

	Mean±SD	Normal Range
n = 17 (8 F)		
Hb (g/L)	139±7.0 155±6.5	120-150 F 130-170 M
Iron levels (umol/L)	16.1±3.6	30-Oct
TSH (mIU/L)	1.7±1.3	0.3-4.5 F
Vitamin D (nmol/L)	52.8±15.3	≥60

Table 3: Demographics and sleep data of for two groups MSL ≤ 8 and MSLT > 8. Results reported as Mean ± SD.

	MSL ≤ 8min (MSLT)	MSL > 8 (MSLT)	P value
N (females)	10 (4 F)	7 (4 F)	
Mean Sleep Latency (MSL)	5.8±1.9	13.1±1.8	< 0.01
Age (yr)	35±10.6	45.0±12.6	NS
BMI (kg/m^2)	26.7±6.6	26.7±5.1	NS
TST (min)	373.8±45.8	361.1±53.1	NS
Sleep onset (min)	19.6±16.8	37.8±51.8	NS
REM Sleep Onset (min)	105.4±41.1	111±68.8	NS
Sleep Efficiency (%)	81.7±9.2	81.8±11.2	NS
Arousal Index AI/hr	7.9±5.5	8.3±5.2	NS
Mean TST - actigraphy (min)	374.5±40.6	354.7±85.3	NS
Mean TST - sleep diary (min)	490.0±84.5	415.1±72.4	NS

16 of the 17 patients had blood tests to measure Haemoglobin, Iron studies, thyroid function and Vitamin D levels. 2/16 (both females) patients had iron levels below 10. Haemoglobin was within normal range for all patients. The majority of patients (14/16) had Vitamin D values below 60 (ranging from 28-87). Refer to (Table 2).

10 out of 17 patients (59%) had a MSL < 8minutes. There was no significant difference in age and BMI; 35.0 + 10.6 *vs.* 45.0 + 12.6 and 26.7 + 6.6 *vs.* 26.7 + 5.1 respectively.

Table 4: Questionnaire and Vitamin D values for the 2 (MSL≤ 8 and MSL> 8).

	MSL≤8min Mean±SD n = 10	MSL>8 Mean±SD n=7	P value
DASS – D	7.8±9.9	8.7±10.3	NS
DASS – A	7.8±7.8	6.0±7.6	NS
DASS – S	13.3±8.9	13.7±14.4	NS
FOSQ	14.7±3.4	14.7±3.1	NS
Fatigue score	5.0±1.2	4.7±1.3	NS
Vitamin D	47.8±11	61±18.8**	NS

** 6/7 patients had a blood test.

The hypersomnolent group (MSLT < 8) slept a total of 373.8 + 45.8 minutes compared to 361.1 + 53.1. Only one patient had one episode of REM sleep onset. (Table 3)

Subjective measurement (sleep diary) of total sleep time was overestimated compared to objective measurement (actigraphy) in both groups by 115 minutes in the hypersomnolent group and 61minutes in the non-hypersomnolent group respectively. Based on actigraphy download, 3/10 patients in the hypersomnolent group (MSL < 8minutes) slept less than 360minutes (mean TST – 297.5, 342.7 and 351.6minutes). Their corresponding mean TST (as per sleep diary) was 430.7, 420minutes. The third patient did not complete their sleep diary. 5/10 patients recorded less than 420minutes on actigraphy and only one patient recorded more than 7hours on actigraphy. One pt had incomplete actigraphy data download.

A DASS- D score of < 20 excludes depressive tendencies. The hypersomnolent group had a mean DASS-D score of 7.8 + 9.9 compared to 8.7 + 10.3 in the non-hypersomnolent group. No significant difference was found in the FOSQ and Fatigue questionnaire scores for the 2 groups.

The patients with an MSL < 8minutes had a Vitamin D level of 47.8 + 11 compared to 61 + 18.8 (Table 4).

Discussion

The assessment of hypersomnia is a complex and labour intensive exercise, requiring comprehensive history taking, exclusion of primary sleep disorders, exclusion of co-morbidities (which can result in daytime fatigue and sleepiness) and exclusion of sleep deprivation as well as performance of polysomnography and MSLT. The diagnosis and management of co-morbidities such as anaemia and thyroid dysfunction is much easier than that of sleep deprivation.

With this in mind, we included routine blood workup, actigraphy and questionnaires (DASS, FOSQ and FQ) in the protocol to more thoroughly investigate the patients.

64 patients were referred for DSS and MSLT during the study period for the assessment of daytime somnolence. 4 declined to participate. 51% of the patients (33/64) patients were not suitable for inclusion in the study due to co-morbidities and medication (antidepressant). 27 patients consented, 3 of which were excluded because they didn't satisfy the inclusion criteria. Of the 24 patients consented, 3 were found to have OSA and were referred for Continuous Positive Airway Pressure (CPAP) trial (one of whom also had iron deficiency). This patient and a second patient with iron deficiency were managed accordingly. Three patients who slept less than 300 minutes, were reviewed and educated on sleep hygiene with close follow up. Patients were reassessed if EDS persisted after treatment for possible medical or psychiatric etiology for fatigue.

After applying exclusion criteria, 17 patients were included in the final analysis. They were a younger group of patients (range 21-61) with 3 patients above the age of 50 and a mean BMI in the slightly overweight range (range 18.7-42.9). 7/17 patients had BMI in the normal range (20-25). 7/17 had BMI in the overweight range and 2/17 had BMI > 30. We found 10/17 had a positive MSL < 8minutes with only one patient having 1REMSO.

In 2015, the National Sleep Foundation released recommendations for sleep duration for young adults (18-25yrs) and adults (26-64yrs) to be 7-9hrs (420-540min) per night [13]. TST on the PSG night varied from 302minutes to 447minutes, with 6/17 patients sleeping less than 6hrs (<360min), 10/17 patients sleeping more than 6hrs and only 3 patients sleeping more than 7hours. No patient slept more than 8hrs. Based on this recommendation only 3/17 patients would be regarded as achieving the recommended sleep time. Two of these three patients had Mean Sleep Latency of < 8minutes and therefore could be considered to be hypersomnolent. The remainders of the 17 patients are sleep deprived and would need to increase their total sleep time before any other management could be considered. In the National Sleep Foundation Poll (2009), 20% of American Adults reported sleeping less than 6hrs per night compared to 35% (6/17) in our cohort (2010-2012) [2].

We know that the measurement of TST is important in the diagnosis of Idiopathic Hypersomnolence (IHS) but can be difficult to assess. TST on the PSG night can be influenced by the patient's sleep/wake cycle leading up to the study night. As such patients were requested to keep a sleep diary for the two weeks leading up to the PSG/MSLT study. Previous literature has shown that patients tend to overestimate their total sleep time when keeping a sleep diary [3]. To verify the patient's sleep/wake cycle, they were asked to simultaneously wear an actigraph band.

We found that patients, in the hypersomnolent group, overestimated their TST reporting a mean of 490 + 84.5 minutes of sleep on their sleep diary *vs.* mean 374 + 40.6 minutes recorded on actigraphy, consistent with previous literature. All patients reported sleeping more than 7-8hours on their sleep diary. If we diagnosed patients solely on the PSG, MSLT and sleep diary, a number of patients might have been labelled as having idiopathic hypersomnolence. The actigraphy download showed 3/10 patients in the hypersomnolent group (MSL < 8minutes) slept less than 360minutes (mean TST – 297.5, 342.7 and 351.6 minutes). Corresponding mean TST (as per sleep diary) was 430.7, 420 minutes. The third patient did not complete their sleep diary. 5 patients slept less than 420 minutes and only one patient slept for more than 7 hours. One pt had incomplete actigraphy data download. The one pt who recorded more than 420 minutes (7hrs) on actigraphy had a MSL 5.8 minutes and one REMSO. Could this 1patient from 64 patients referred for DSS + MSLT be labelled with Idiopathic Hypersomnolence in accordance with ICSD-3? [14]. The remaining patients could improve their sleep duration.

The added information provided by actigraphy was found to be useful in confirming/excluding sleep deprivation in turn determining appropriate patient management. The actigraphy data was a useful tool in educating patients regarding their sleep hygiene.

An interesting finding was that 12/16 patients (one pt did not have a blood test) showed Vitamin D levels below 60nmol/L. 9/10 patients in the hypersomnolent group had a Vitamin D value below 60nmol/L.

The association between Vitamin D and daytime fatigue is unclear but there is mounting evidence in the literature regarding the role of Vitamin D and daytime fatigue. McCarty et al., [15] discussed the possible pathways linking low Vitamin D levels to impaired wakefulness. The authors concluded that "abnormally low levels of Vitamin D are common in populations seeking care for sleep-medicine complaints, and may be causes or contributors to common sleep-disorder symptoms including chronic nonspecific pain, reduced subjective sleep quality and impaired experience of wakefulness."

The impact of the low vitamin D in our patients is difficult to assess but unlikely to be the cause for their EDS, however, correction of the low Vitamin D levels should be addressed.

Further studies are required to assess the impact of correcting Vitamin D levels on daytime fatigue. MET is the metabolic equivalent of task. 1 MET equals the energy to lie/sit quietly. According to the Canadian Academy of Sports and Exercise Medicine <1.6METs is classified as sedentary and 1.6-3.0Mets as Light intensity activity. Sitting and reading, watching TV or driving are examples of sedentary activity/intensity [16].

The mean METs recorded for the 17 patients (1.5 + 0.28) places them in the sedentary (<1.6Mets) to light range (1.6-3.0Mets) of activity. Examples of light intensity are slow walking (e.g. for example around the house) and light work while standing (cooking, washing dishes), playing an instrument. It is not unreasonable to hypothesise the low METS and Vitamin D values are consistent with hypersomnia and reduced outdoor activity. Further studies to address the interaction between Vitamin D and the degree of activity in these patients are required.

Conclusion

Many patients present to the Sleep Clinic complaining of daytime somnolence. There are many causes for excessive daytime somnolence which need to be assessed, with sleep deprivation being a common cause. The use of actigraphy was helpful in the objective measurement of TST, identifying 8/9 patients in the hypersomnolent group slept less than 7 hours. As per current guidelines, these patients are sleep deprived and would benefit from sleep hygiene management before stimulant medication could be considered.

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