Sleep Characteristics in Postural Orthostatic Tachycardia Syndrome

Okeanis Vaou1*, Andrew J Westwood1, Yelena Gorfinkel-Pyatkevich3, Sanford H Auerbach3, and Anna DePold Hohler3

1Department of Neurology, Noran Neurological Clinic, USA
2Department of Neurology, Columbia University, USA
3Department of Neurology, Boston University School of Medicine, USA

Abstract

Study Objectives: Patients with Postural Orthostatic Tachycardia Syndrome (POTS) complain of difficulties with sleep dysfunction. This study characterizes sleep architecture and Alpha-Delta sleep (ADS) in patients with POTS.

Methods: Patients diagnosed with POTS with reported daytime sleepiness were evaluated by polysomnography (women=100%; mean age= 34.3; range 25-55). Measurements included number of nocturnal awakenings as well as the average hours of sleep, sleep architecture, alpha wave intrusion in NREM (N3) sleep efficiency and apnea-hypopnea index and sleep stages.

Results: Sleep efficiency was reduced (62.02%, range=47.6-78.1) with prolonged REM latencies (229.8 minutes, range 127.5-404.5) and increased N2 sleep (69.22%, range 61.1-79.9%). Decreased REM sleep (8.72%, range 1.5-17.3) and decreased REM cycles (1.2, range 1-2) were observed (0.46, range 0-1.6).

Conclusions: In this study POTS patients were noted to have abnormal sleep architecture and alpha delta sleep.

INTRODUCTION

Postural orthostatic tachycardia syndrome (POTS) is a dysregulation of the autonomic nervous system and is defined as symptomatic orthostatic intolerance associated with a heart rate increase of 30 bpm (or exceeding 130 bpm) within the first 10 minutes of standing or upright tilt, not associated with other chronic debilitating conditions or medications known to diminish vascular or autonomic tone, and in the absence of orthostatic hypotension [1]. Typically it affects women more than men with a male: female ratio 4.5:1, usually between ages of 15-25 years. Often unrecognized and misdiagnosed, POTS may produce substantial disability among otherwise healthy people [2]. Patients with POTS commonly complain of wide ranging symptoms including palpitations, fainting, tremors, gastrointestinal pain and migraines. Sleep complaints are also reported including fatigue, non-restorative sleep and daytime sleepiness. In a large series of adult patients with POTS, 32% reported sleep disturbances [3]. Typically patients describe themselves as light sleepers. A recent study showed that sleep problems in POTS can significantly contribute to a diminished quality of life: ~50% of the variability in health related quality of life can be explained by the variability in sleep problems [4]. Autonomic dysregulation is one of the hallmarks of the disease and this may underpin the sleep complaints reported. In healthy individuals, non-rapid eye movement (NREM) sleep is characterized by relative autonomic stability, a dominance of parasympathetic influences to the heart, and a reduction in sympathetic efferent vasomotor tone, all of which translate into a stable low heart rate and low blood pressure. In contrast, rapid eye movement (REM) sleep is a state of autonomic instability, dominated by remarkable fluctuations between parasympathetic and sympathetic influences, which produce marked sudden changes in heart rate and blood pressure [5]. Alpha-delta sleep (ADS) is described as alpha wave intrusions in delta NREM (N3) sleep and has been observed in patients with fibromyalgia, depression and chronic fatigue in non-depressed patients who share similar sleep complaints with POTS patients. Alpha-delta sleep was first described in 1973 in patients with psychiatric disorders [6]. We hypothesized that ADS would be observed in patients with POTS based on the chief complaint of non-restorative sleep. Given the common reports of sleep disruption and the close relationship of sleep with the autonomic system, we hypothesized that sleep parameters would be abnormal in patients with POTS. Here we describe a case series and identify features of sleep using polysomnograms to assess the sleep characteristics and presence of ADS in this population.

METHODS

This study was approved by our institutional IRB. Polysomnography was conducted at the Sleep Medicine Center at Boston Medical Center. All patients presented with clinical sleep disturbances of non-restorative sleep and a concomitant diagnosis of POTS. Patients who met criteria for POTS based on tilt table testing and clinical evaluation by an autonomic specialist in the outpatient clinic were referred to a board-certified sleep physician for their sleep complaints of non-restorative sleep and sleep maintenance insomnia. Only patients 18 years and older who had polysomnograms were selected. We included subjects with at least 6-months of symptoms in the absence of another chronic debilitating disorder or prolonged bed rest. Patients with known obstructive sleep apnea, depression/ anxiety, fibromyalgia, chronic fatigue syndrome, pain or patients who were on chronic selective serotonin reuptake inhibitors were excluded from the patient’s studies. All five patients were treated with β-blockers for POTS. Subjects underwent diagnostic digital polysomnography (PSG) with the simultaneous recording of electroencephalogram, electro-oculogram, electromyogram, electrocardiogram, respiratory effort, thermistor respiratory flow, nasal pressure, pulse Oximetry, leg movement, body position, sound and video. The data was adequate for interpretation; sleep scoring followed the standard put forth by the American Academy of Sleep Medicine (AASM) [5]. PSGs were scored manually by a registered PSG technician in accordance to the 2007 AASM scoring criteria [5].

Alpha-delta sleep was defined by the duration of delta waves in NREM (N3) sleep superimposed by alpha waves and then divided by the total slow wave sleep multiplied by 100. All NREM epochs were manually scored for alpha and delta frequency waves. Alpha and delta waves are defined as a frequency of 8-13 cycles per second and 0.5-2 cycles per second respectively and were scored manually by one sleep specialist [7].

RESULTS

Six subjects met our selection criteria (women=100%; mean age= 34.3; range 25-55). Based on findings on the polysomnography, 1 patient was excluded from the study due to the diagnosis of mild obstructive sleep apnea.

Polysomnogram Data

Data was compared to the established normative data for polysomnography in adults which suggest wakefulness <5%, N1 2-5%, N2 45-55%, N3 13-23%, REM 20-25% and REM cycles 4-6/night [8,9]. A detailed list of sleep parameters for the individual patients is displayed in Table 1. All patients showed reduced sleep efficiency (62.02%, range=47.6-78.1) with prolonged REM latencies (229.8 minutes, range 127.5-404.5), increased N2 sleep (69.22%, range 61.1-79.9%), decreased REM sleep (8.72%, range 15.7-17.3) and decreased REM cycles (1.2, range 1-2) despite a normal AHI (0.46, range 0-1.6). All five patients were found to have ADS (7.32%, range 3-16.5%). Sleep efficiency was reduced in all patients. Those with greater sleep efficiency had a lower percentage of ADS. No correlation was observed between ESS and ADS in contrast to previously published data of a positive correlation between the two [7]. Four of the five patients were slim with only one patient with a high body mass index (BMI) of 38. Reduced BMI is usually seen in patients with POTS. A recent study showed no correlation between total sleep time and BMI among insomniacs but found a negative correlation between the amount of slow wave sleep (SWS) and BMI in the same population. Our population had normal amount of SWS [10].

DISCUSSION

This study is novel in characterizing the objective sleep patterns and ADS in POTS using polysomnography. All subjects reported daytime sleepiness and fatigue as well as non-restorative sleep. Our patients had an increased number of nocturnal arousals and decreased sleep efficiency compared to the normative data. The sleep staging and architecture was notable for an increase in REM sleep latency, and a greater amount of N2 stage sleep. We also found a decreased amount of REM sleep and REM cycles. Alpha intrusion in slow delta wave sleep was noted on all five polysomnograms. This has been linked to the sensation of “light, easily arousable sleep” [11]. The patients with greater sleep efficiency had a lower percentage of ADS. No correlation was observed between ESS and ADS. In a study by Manu et al [12], alpha-delta sleep was significantly more common among patients who had chronic fatigue without major depression. In a study by Branco et al [13] almost all of the fibromyalgia patients studied had increased alpha-delta sleep and complaints of nonrestorative sleep. In our cohort, none of the patients had a diagnosis of depression, chronic fatigue syndrome or fibromyalgia and were not taking any medication which could alter sleep architecture such as selective serotonin re uptake inhibitors (SSRIs), tricyclic antidepressants (TCA) or benzodiazepines. A study by McClelland et al [14] found that

| Table 1: Sleep Parameters obtained during in-lab polysomnography. |
|--------------------|-------|-------|-------|-------|-------|
| Patient            | SL (minutes) | REM L (minutes) | BMI | TST (minutes) | SE (%) |
| 1                  | 56.5 | 209 | 21.3 | 231.5 | 62.2 |
| 2                  | 42.5 | 127.5 | 21.4 | 306.5 | 69.5 |
| 3                  | 9 | 404.5 | 21.3 | 69.6 | 78.1 |
| 4                  | 25.5 | 246 | 21.3 | 208 | 49.2 |
| 5                  | 117.5 | 163 | 18.4 | 211.5 | 51.1 |

Abbreviations: BMI: Body Mass Index; TST: Total Sleep Time; defined as time asleep in bed; SE: Sleep Efficiency, defined as TST/Time in Bed; SL: Sleep Latency, defined time to persistent sleep; REM L: REM latency, defined as time to REM; N1: Non-REM stage 1 sleep; N2: Non-REM stage 2 sleep; N3: Non-REM stage 3 sleep; REM: Rapid Eye Movement sleep stage; TLM (A): Total Limb Movements (Average); ADS- Alpha Delta Sleep. Stages of sleep as defined by AASM
treatment with duloxetine in normal subjects reduces alpha waves and increases delta waves in sleep. Therefore, if indeed treatment with SSRIs decreases ADS, this may play an important role in improving sleep in patients with POTS. In a recent study of by Bagal et al [15] thirty six patients with POTS with sleep complaints and thirty six healthy subjects were studied using wrist actigraphy. The study showed a correlation of high nor epinephrine and actigraphic sleep onset latency. This hyper adrenergic state may contribute to the subjective and objective sleep disruptions in POTS patients. Sympathetic-nerve activity, blood pressure, and heart rate are lower in normal subjects while they are in deep non-REM sleep than while they are awake. Arousal stimuli during non-REM sleep elicit K complexes, which are accompanied by bursts of sympathetic-nerve activity and transient increases in blood pressure. During REM sleep, sympathetic-nerve activity increases above the levels recorded during wakefulness, and the values for blood pressure and heart rate return to those recorded during wakefulness. Momentary restoration of muscle tone during REM sleep (REM twitch) is frequently associated with cessation of sympathetic-nerve discharge and increases in blood pressure [6]. This study has some limitations. First, our sample size is relatively small, and as this is a preliminary study, there is no control group. Due to the limited number of patients and the retrospective design, it is difficult to draw reliable conclusions based on statistical models. We report though a positive trend with our findings. However, in spite of this it is still one of the largest studies to thoroughly study this patient population, and the only one thus far to include tilt testing, PSG, and actigraphy. The interpretation and scoring of alpha-delta sleep was performed by one reader only. However due to the limited sample and the retrospective design of this study, it is difficult to draw reliable conclusions based on statistical models. Finally, subsequent studies might include two consecutive PSGs to reduce the impact of the first night effect which may interfere with the results. The findings of this study indicate a consistently high prevalence of nocturnal arousals coinciding with complaints of non-restorative sleep and daytime sleepiness and correlating with ADS. The low sleep efficiency index and the high number of arousals objectify the subjectively presented complaints of a distorted sleep pattern and non-restorative sleep. A future study aimed at consolidating sleep, could improve the quality of life in these patients. Aerobic exercise, or sympatholytic agents such as clonidine or methyldopa may provide symptomatic relief in patients with POTS [11]. Recent development of pure heart rate reductive medication, such as ivabradine, is worth exploring on prospective trials for patients with POTS [16]. A correlation between the severity of POTS symptoms, norepinephrine levels, and sleep dysfunction and ADS may aid in better understanding the contribution of the hyperadrenergic state in POTS and sleep. More studies should be performed on the effect of SSRIs on sleep architecture and ADS. If they decrease alpha-delta sleep, this may be beneficial in improving sleep in patients with POTS. Furthermore, ADS could be used as an additional marker or criteria in the diagnosis of POTS.

**AUTHOR CONTRIBUTIONS**

Study concept and design: Vaou, Hohler; Acquisition of data: Vaou, Gorfinkel-Pyatkevich, Auerbach; Analysis and interpretation of data: Vaou, Westwood, Gorfinkel-Pyatkevich; Draft of the manuscript: Vaou, Westwood. Critical revision of the manuscript for important intellectual content: Hohler, Auerbach;

**REFERENCES**


Cite this article