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Pediatric sleep and autonomic complaints

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Kaitlyn Gundrum[1], Thomas C Chelimsky[1], Nan A Norins[1], Pippa Simpson[1], Melodee Nugent[1] and Gisela Chelimsky[1,2]

Abstract

Objectives: Little is known about the relationship between autonomic dysfunction and sleep disturbances. This study aimed to identify patterns of sleep disturbances and autonomic dysfunction in children.

Methods: A retrospective chart review of 14 children who underwent sleep and autonomic testing was performed. Subjects were divided into three groups based on sudomotor Composite Autonomic Severity Score Scale score and postural tachycardia syndrome criteria. Sleep quality, sleep architecture, and number of comorbidities were analyzed.

Results: There were no statistically significant differences between groups in measures of sleep quality, sleep architecture, and number of comorbidities.

Conclusion: Patients with postural tachycardia syndrome and autonomic dysfunction experience multiple sleep-related complaints. The low power of our study did not allow firm conclusions, but there is no pattern to these abnormalities.

Keywords

Postural tachycardia syndrome, sleep disturbance, autonomic dysfunction

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Background

Postural orthostatic tachycardia syndrome (POTS) is defined as a sustained increase in heart rate of greater than 40 beats per minute within 10 min of the head-up tilt in the absence of a drop in systolic blood pressure of 20 mm Hg or diastolic 10 mm Hg.[1] Common symptoms associated with POTS include dizziness, lightheadedness, nausea, constipation, and migraine headache.[2] Most pediatric POTS patients complain vociferously of fatigue (>90%) and sleep disturbances (>70%) as their most disabling issues.[3] Adults with POTS have significantly more sleep problems than the general population which decrease their quality of life.[4,5] These include subjective daytime sleepiness, more fatigue levels, and more sleep problems.[4] Polysomnography showed that total sleep time included a significantly higher proportion of stage 2 sleep, implying that their sleep is generally "lighter" than normal. In addition, heart rate variability during sleep showed diminished low- and high-frequency responses when compared to healthy controls (HCs).[5] Interestingly, a different study comparing adult patients with POTS to other patients referred to the sleep lab did not show that the sleep complaints of the POTS group were a consequence of any sleep-related disorder.[6] Given these findings, as well as previous descriptions of the multiple comorbid conditions of POTS,[2,3] the sleep complaints could reflect central hypervigilance rather than a genuine abnormality of sleep physiology. This information is important, since a sleep issue will typically require a specific medical approach that may not be currently in use, while central hypervigilance will benefit from most of the approaches already in use for POTS, including cognitive behavioral therapy, increased physical activity, and some pharmacologic support such as beta blockers.

Based on the current literature, we hypothesized that children with POTS would demonstrate no traditional sleep disorder compared to children without POTS, and that the sleep complaints might reflect either a central hypervigilance phenomenon[7] or a higher proportion of "lighter" sleep stages throughout the sleep cycle as found by others. This study is driven in particular by the high frequency of these complaints,

[1]Medical College of Wisconsin, Milwaukee, WI, USA
[2]Division of Pediatric Gastroenterology, Medical College of Wisconsin, Milwaukee, WI, USA

Corresponding author:
Gisela Chelimsky, Division of Pediatric Gastroenterology, Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI 53226, USA.
Email: gchelimsky@mcw.edu

absence of studies, and close physiologic relationship between sleep and autonomic function.[8,9] This study also aimed to identify any relationship between any pattern of sleep disturbance and the pattern of autonomic dysfunction (e.g. mainly cardiovascular findings as seen in POTS vs mainly an autonomic neuropathy with or without POTS).

Inclusion into this Institutional Review Board–approved retrospective chart review required the presence of both autonomic testing at Children's Hospital of Wisconsin (CHW) and Froedtert Memorial Lutheran Hospital (FMLH) or at another institution with results available in our medical records at either CHW or FMLH between September 2004 and February 2013 and a sleep study. Of 19 patients who met criteria for this study, 3 were excluded for multiple congenital abnormalities and 2 because of generalized patient noncompliance and prolonged awakenings of clear behavioral origin.

Patients were divided into three groups based on their autonomic testing results. The degree of neuropathy was measured using quantitative sudomotor axon reflex tests (QSARTs) and graded using the sudomotor index of the Composite Autonomic Severity Score (CASS) Scale.[10] Patients were then divided into three groups: (1) minimal findings group ("minimal") without POTS and with a sudomotor CASS of 0–1, (2) moderate findings group ("moderate") without POTS and a sudomotor CASS of 2–3, and (3) POTS± group ("POTS±") with POTS, regardless of sudomotor CASS. In summary, the minimal findings group had no significant autonomic issues, the moderate findings had an autonomic neuropathy without POTS, and the POTS± group had POTS and could also have an autonomic neuropathy.

All subjects underwent overnight polysomnography in the CHW sleep lab, accredited by the American Academy of Sleep Medicine (AASM). Tracings were scored in 30-s epochs using staging and scoring criteria as outlined in *The AASM Manual for the Scoring of Sleep and Associated Events*. Board-certified sleep physicians reviewed the raw data and interpreted the results. In sleep studies performed before 2007, sleep stages NREM 1 analyzed as N1, NREM 2 analyzed as N2, and NREM stage 3 and 4 were added together and analyzed as stage N3, as per current AASM sleep study classification.

For every patient, the following data were collected: chief complaint at time of testing, autonomic testing diagnosis, sleep study diagnosis, gender, age, body mass index (BMI), migraine history, comorbid diagnoses, and medications at time of sleep testing. Sleep study data included the following: respiratory rate; oxygen saturation; end-tidal carbon dioxide; heart rate; total recording time; total sleep time; sleep latency; rapid eye movement (REM) latency; prolonged awakenings; wake time after sleep onset; percent of stages N1, N2, and N3 sleep; percent of REM sleep; number of obstructive apneas; mixed apneas; hypopneas; central apneas; apnea–hypopnea index; REM apnea–hypopnea index; morning capillary blood gas pH; pCO2; HCO3; base excess/deficit; arrhythmias; periodic limb movement; and periodic limb movement index. Seven patients also had multiple sleep latency test (MSLT) data which included the following: number of naps taken, sleep latency, REM periods, urine drug screen, and medications at time of testing. Sleep studies were then read as normal or abnormal based on presence of sleep-related breathing disorder and/or periodic limb movement disorder, MSLT results, as well as sleep architecture using established age-dependent sleep norms.[11]

Comorbid diagnoses were identified through problem lists and visit diagnoses in the medical record. Comorbidities of importance included the following: cyclic vomiting syndrome (CVS), gastroesophageal reflux disorder (GERD), constipation, functional abdominal pain, chronic fatigue, fibromyalgia, hypermobility, depression, anxiety, attention hyperactivity disorder (ADHD), abdominal pain, weight loss, syncope, heat intolerance, Von Willebrand disease, asthma, autoimmune lymphoproliferative syndrome (ALPS), autism, seizures, type I diabetes, eosinophilic esophagitis, epilepsy, irregular menstruation, chest pain, Osgood–Schlatter disease, scoliosis, Ehlers–Danlos syndrome, and Tourette's syndrome.

The absence of healthy controls (HCs) in this retrospective chart review was partially mitigated using a literature comparison from Antelmi et al.[12] HC control values are added in italics next to our cohort values where available. SPSS® (IBM Corporation, Armonk, NY, USA) was used to analyze the data (Version 22; Chicago, IL, USA). Fisher's exact test was used to compare categorical variables, and the Mann–Whitney test was used to compare two continuous variables (Kruskal–Wallis test was used to compare more than two groups). A p value of <0.05 was considered significant. Given the exploratory and "case-series" nature of the study, no sample size analysis was performed.

Results

Table 1 summarizes the demographic data of the 14 included subjects, with no significant differences in age, BMI, and gender distribution. Sleep efficiency had a median (range) of 83% (77%–95%) in minimals, 91% (73%–99%) in moderates, and 87% (64%–97%) in the POTS± group, $p = 0.68$. REM sleep had a median (range) of 18% (16%–20%) in minimals, 23% (6%–29%) in moderates, and 19% (11%–37%) in the POTS± group, $p = 0.70$ (HC = 22.1 ± 5.6 SD (standard deviation)).[12] Deep sleep (stage N3) had a median (range) of 18% (13%–19%) in minimals, 21% (13%–25%) in moderates, and 15% (13%–27%) in the POTS± group, $p = 0.99$ (HC = 24.1 ± 7.6 SD).[13] One patient met diagnostic criteria for mild sleep apnea, one patient met criteria for borderline periodic limb movement disorder, and one patient met criteria for idiopathic hypersomnia. The number of comorbidities had a median (range) of 5 (3–9) for the minimals, 5.5 (3–9) for moderates, and 6.5 (1–14) for POTS± group, $p = 0.78$ (Table 2).

Table 1. Demographics by group.

	Minimal		Moderate		POTS±		P value
	N	N (%) or median (range)	N	N (%) or median (range)	N	N (%) or median (range)	
Gender	4		4		6		0.63
Male		2 (50)		3 (75)		5 (83)	
Female		2 (50)		1 (25)		1 (17)	
Age (years)	4	16.5 (11–18)	4	14.5 (5–18)	6	15 (12–18)	0.85
BMI	4	22.8 (19.9–31.0)	4	19.8 (15.6–24.2)	6	23.3 (19.8–27.0)	0.27

POTS: postural tachycardia syndrome; BMI: body mass index.

Discussion

Besides their chief complaint of orthostatic intolerance, sleep and fatigue probably rank as the most common and disabling complaints in children with POTS.[3] Thus, it is quite surprising that this is the first study to examine their sleep disturbances, much more given the association of sleep with fatigue, migraines,[13,14] and chronic pain,[15] so frequently present in POTS and patients with dysautonomia. In summary, we found that sleep abnormalities do not differ across groups with different autonomic abnormalities. Specifically, there was no difference in measures of sleep onset latency, wake time after sleep onset, or sleep efficiency, probably the most commonly used measure of objective sleep quality, nor in measures of sleep architecture, including percent of stage N3 sleep and percent of REM sleep. This parallels the known sleep-state misperception that has been documented in adult POTS patients.[4,16] Finally, we also saw no difference in the number of comorbidities among the groups. Unlike previous studies which compared patients with autonomic complaints to HCs, subjects in this study were compared to other subjects who had sleep and autonomic complaints.

Our study findings parallel those studies in adults where multiple sleep abnormalities were detected in the dysautonomia population with no specific pattern in sleep architecture or underlying sleep disorder.[6] Although adult POTS patients have lower sleep efficiency than their healthy counterparts,[16] it remains unknown whether this lower sleep efficiency is truly conferred by the diagnosis of POTS per se or simply accompanies complaints of orthostatic intolerance and/or the comorbid disorders of POTS. This study design addresses this gap by comparing POTS to non-POTS in groups with similar clinical presentations. In this context, we do not find any trends or differences in sleep efficiency across groups. While subjective sleep-related complaints are prevalent in this population, there is an absence of any objective sleep study results or findings. Perhaps this sleep study technology lacks the physiologic sophistication to identify actual sleep differences between these groups, or perhaps these sleep-related complaints are actually due to alterations in aspects of daytime function that we usually attribute to sleep but are in fact caused by some other autonomic dysfunction.

The number of comorbidities did not vary significantly between autonomic groups. This suggests that autonomic testing is not an effective predictor of symptom burden. Furthermore, the wide range of comorbidities reported in these patients suggests that POTS may not be the single physiologic underpinning of orthostatic intolerance but reflective of a more complex syndrome involving multiple pathways and organ systems as previously suggested by Ojha et al.[2] Just as the presence of POTS on autonomic testing does not drive other comorbidities,[3] it appears not to be driving the sleep disorders, based on the absence of any correlation in this study.

The findings of this study are of critical importance to general practitioners. Although ideally this study should be followed by a prospective study with age-matched HCs, the findings suggest that performing polysomnograms in children with POTS without some other more specific set of classical sleep-related symptoms such as obstructive apneas or periodic limb movements will likely not elucidate the sleep complaints.

This study has several limitations, the most critical being the small number of patients that met inclusion criteria (n = 14). The decision was made not to parse out the small groups any further, so standard numbers for normal percentages of sleep stages were used. Therefore, minor differences across the pediatric age span in sleep architecture were not accounted for in overall data analysis. In addition, the retrospective nature of this study could have led to selection bias. In support of our findings, usually sleep studies are done only when the sleep complaints are significant enough to affect daytime function. Therefore, only patients with the most severe dysfunction would be in this study. However, this could also be considered a strength, since this is where we might expect to see a difference if one existed.

In summary, this is the first study to examine autonomic dysfunction and sleep disorders in a pediatric population. These data support the concept that patients with orthostatic complaints with or without POTS suffer involvement of multiple organ systems, including sleep in some, yet, no particular sleep disorder appears to either characterize the group or parse with the physiologic POTS diagnosis. This occurrence of sleep abnormalities without a particular pattern matches findings in the adult population.[5,16] POTS is likely a complex

Table 2. Subject characteristics.

ID	Autonomic diagnosis	Chief complaint	Sleep comments	Gender/ age	BMI	No. of comorbidities	Sleep latency (min)	REM latency (min) (83.7 ± 39.7)	Sleep efficiency % (91.2 ± 9.7)	Stage N3 % (24.1 ± 7.6)	REM % (22.1 ± 5.6)
Minimal group											
1	Normal autonomic, neuropathy CASS 1	Fatigue, chronic headaches	Increased stage N1 sleep	M, 18	23.1	5	3	90	95	13	20
2	Normal	Syncope	Increased stage N1 sleep, fragmented sleep architecture, two prolonged awakenings	F, 17	31.0	5	0	75	82	19	17
3	Normal	Migraines, morning sleepiness	Increased stage N1 sleep	F, 11	19.9	9	8	298	83	19	16
4	Normal autonomic, neuropathy CASS 1	Migraine, fatigue, muscle aches	Mild obstructive sleep apnea	M, 16	22.5	3	108	53	77	18	20
Moderate group											
1	Neuropathy CASS 3	Desaturations, disordered breathing	Neurological movement disorder	M, 5	15.8	5	0	88	99	25	29
2	Neuropathy CASS 2–3	Daytime sleepiness	Increased stage N1 sleep, MSLT with daytime sleepiness, unsure whether significant due to tape/monitor discomfort	F, 18	24.2	3	18	154	73	18	6
3	Neuropathy CASS 2	Chest pain, sleepiness	Increased stage N1 sleep	F, 17	21.6	9	25	93	85	13	21
4	Neuropathy CASS 2	Benign rolandic epilepsy, sleepiness	Normal study	F, 12	18.0	6	8	58	97	23	25
POTS± group											
1	POTS, syncope	Insomnia, "electric feeling in legs"	Sleep test performed at age 13 with autonomic symptoms, increased stage N1 sleep, borderline periodic limb movement disorder	F,18	27.0	4	33	104	87	13	17
2	POTS, neuropathy CASS 2	Heat intolerance, migraine, fatigue	Increased daytime sleepiness, MSLT normal	F,12	24.3	6	37	110	88	22	18
3	POTS, neuropathy CASS 2	Migraine, joint pain, fatigue	Borderline Increased stage N1 sleep	F, 16	22.2	2	41	79	65	14	37
4	POTS, syncope, neuropathy CASS 2	Reflux, apnea	MSLT showed idiopathic hypersomnia	F, 15	19.8	2	6	176	97	27	21
5	POTS, syncope, neuropathy CASS 2	Syncope, sleepiness	Increased stage N2 sleep	F, 15	21.6	5	16	137	87	14	14
6	POTS, neuropathy CASS 1	Apnea, psychiatric problems	Repetitive awakenings	M, 14	25.4	14	29	72	64	17	11

BMI: body mass index; REM: rapid eye movement; stage N1: non-rapid eye movement stage 1; stage N2: non-rapid eye movement stage 2; stage N3: deep sleep, composed of non-rapid eye movement stages 3 and 4; CASS: Composite Autonomic Severity Score; MSLT: multiple sleep latency test. In ( ) are the values from healthy controls described by Antelmi et al.[12]

Value greater than normal range	
Value less than normal range	

syndrome involving multiple systems with varied pathophysiology. From a clinical perspective, the important points include the following: (1) the vast majority of pediatric patients with POTS complain of fatigue or sleep disruption as their "second" chief complaint[3] and (2) yet sleep studies may provide little useful information unless the patient has a clearly defined unrelated sleep diagnosis, an uncommon occurrence (here, mild sleep apnea × 1 and restless legs × 1).

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Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

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Informed consent

Since this was a retrospective chart review, there was a waiver of consent.

Trial registration

This study was not registered in as any trial.

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