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Beyond a motor disorder: A prospective evaluation of sleep quality in cervical dystonia

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ABSTRACT

Background: Little is known about sleep disturbances in cervical dystonia (CD), particularly the relationship to motoric symptoms. It is critical to clarify these points given the impact on quality of life.
Methods: Primary CD patients receiving botulinum toxin (BoNT) injections and age- and gender-matched healthy controls were included. In both groups, sleep quality and daytime sleepiness were assessed. In CD, these assessments were repeated following BoNT injections. CD severity, mood symptoms, and health impact of CD were also assessed.
Results: 54 CD patients and 55 controls were included. Impaired sleep quality was more frequent in CD compared to controls ($t = 4.82$, $p < 0.0005$), even when controlling for the effects of depression, anxiety, and benzodiazepineuse ($F = 5.62$, $p = 0.020$). Excessive daytime sleepiness was not significantly different between groups ($t = 1.67$, $p = 0.1$). 48 patients received BoNT and returned for follow-up. There was no improvement in sleep quality ($t = 0.834$, $p = 0.41$) or daytime somnolence ($t = 1.77$, $p = 0.083$) despite improvement in CD severity ($t = 4.77$, $p < 0.0005$) with BoNT. There was a small improvement in health impact ($t = 2.10$, $p = 0.04$).
Conclusion: Sleep quality was more impaired in CD patients, compared to healthy subjects, and did not improve following BoNT treatment, despite a robust improvement in CD severity. This dichotomy suggests that sleep aberrations in CD require separate focus for effective treatment and cannot be viewed as secondary complications of the motor elements of this condition.

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1. Introduction

Cervical dystonia (CD) is a focal dystonia that causes abnormal postures of the head, neck, and shoulders and is often associated with pain. These clinical attributes of involuntary movement and pain have been considered the primary contributors to disability in CD [1,2]. However, recent studies have described non-motor features of dystonia, including depression, anxiety, and sleep disturbances that may be additional factors impacting disability and quality of life in dystonia [3,4]. The specific aims of this study are to investigate the frequency of sleep disturbances in CD compared to an age- and gender- matched control group as well as to study the association of motoric treatment on sleep disturbances.

To date, only a few studies have assessed sleep in individuals with CD, without a unifying conclusion. Two recent studies suggested an increase prevalence of sleep disturbances in CD; however, this was in part due to the confounding effect of depression [5,6]. Further, control participants were not matched for gender suggesting that comparisons of sleep disturbances between the two groups were imprecise. It is likely that the prevalence estimate of sleep disruptions in CD compared to controls was overestimated as the majority of CD participants were female [6] and there is a well-established increase in sleep disturbances in females of this age range compared to males [7]. Additionally, as these studies were cross-sectional, the association of sleep disturbances with motor severity and the effects of motoric treatment have not been defined. The first step, therefore, in establishing the relationship between CD and sleep alterations is to establish if sleep disturbances are truly more prevalent in CD patients compared to age- and gender-matched healthy controls. If so, the second step is to establish if there is an independent treatment effect of botulinum toxin (BoNT) therapy, the mainstay of treatment for CD. Clarifying these points are essential as clinicians often focus their therapeutic efforts on treatment of motor symptoms, considering non-motor features as secondary consequences. In an attempt to clarify these unresolved issues and to guide clinicians in treatment recommendations, we

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prospectively studied sleep quality in a clinically well-defined cohort of focal CD patients over the course of a single BoNT treatment cycle.

2. Methods

2.1. Patients and controls

CD subjects were recruited consecutively over a 7-month period at the Rush University Movement Disorder Center BoNT treatment clinic. Subjects were included for participation if they were over the age of 18 years, had a diagnosis of primary CD made by a movement disorder specialist, and were receiving serial BoNT treatment. Those with a history of a clinical remission were excluded from the final analysis, as it was felt that these subjects would not be representative of a true treatment effect. Subjects were excluded if they had clinically significant dystonia in other body areas, prior surgical treatment for CD, and previously diagnosed sleep disorders. Healthy controls without CD, other neurological, or primary sleep disorders were recruited from an Internal Medicine practice at Rush University Medical Center. Informed consent was obtained for all subjects. The study was approved by the Institutional Review Board at Rush University.

2.2. Interviews, examinations, and self-rating measures

Demographic information, including age, gender, and concomitant medications was obtained from both CD patients and healthy controls. Additional information obtained from the CD patients included CD duration and date of last BoNT injection. Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI), a validated scale that assesses seven domains of sleep (sleep efficiency, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleep medication, and daytime dysfunction), with cumulative scores greater than 5 suggestive of sleep impairment [8]. Excessive daytime sleepiness was assessed using the Epworth Sleepiness Scale (ESS), a validated measure that asks respondents to rate their usual chances of falling asleep during certain situations, with cumulative scores greater than 10 considered abnormal [9,10]. CD severity was assessed using the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS), a validated measure that evaluates severity, disability, and pain associated with CD [11]. The health impact of CD was assessed by the Cervical Dystonia Impact Profile (CDIP-58). The CDIP-58 is a validated measure that evaluates the health impact of CD in 8 domains (head and neck symptoms, pain and discomfort symptoms, upper limb activities, walking, sleep, annoyance, mood, and psychosocial functioning), with higher scores indicating worse health [12]. The Beck Depression Inventory-II (BDI) was used for the evaluation of depressive symptomatology, with cumulative scores of 0–13 considered minimal, 14–19 mild, 20–28 moderate, and 29–63 severe [13]. The Hamilton Anxiety Rating Scale (HAM-A) screened for symptoms of anxiety, with cumulative scores of 18–24 indicating mild to moderate severity and 25–30 indicating moderate to severe anxiety [14]. In CD patients all measures were completed at baseline prior to BoNT injection, defined as study start, and at 6–8 weeks follow-up. A 6–8 week interval was chosen to reflect the peak effect of BoNT. In controls the PSQI, ESS, BDI, and HAM-A were completed at the study visit.

2.3. Statistical analysis

We selected a sample size of 45 CD patients and 45 control patients in order to have sufficient power ($1 - b = 0.85$) to detect a change in PSQI of approximately 0.64 standard deviations (effect size $d = 0.639$), corresponding to approximately 4.5 points on the PSQI with alpha set at 0.05, using a t statistic (critical $t = 1.99$ with 88 degrees of freedom).

Data was analyzed with SPSS version 18.0 (SPSS, Inc., Chicago, IL). Comparison of sleep disturbances and mood symptoms in CD patients versus controls was performed by the independent samples t test. Changes in sleep disturbances, CD severity, and mood symptoms from baseline to follow-up in CD patients were assessed with the paired t test. A Mann–Whitney analysis was employed to compare the subcomponents of the PSQI in CD patients to controls. To control for the potential confounding effects of depression, anxiety, and benzodiazepine use, an Analysis of Covariance (ANCOVA) was utilized. Demographic and disease-related variables were summarized using descriptive statistics.

3. Results

3.1. Patient and control samples

Our study included 54 primary CD patients (80% female, mean age of 62 years (SD 10.1), mean duration of CD was 18.7 years (SD 14.7)). One patient was excluded from the final analyses due to a clinical remission. On average participants were 15.3 weeks (SD 4.0) out from their last injection. Thirty-five percent of CD patients were on benzodiazepines (of which 24% were on clonazepam), 4% on anticholinergics, 7% on baclofen, and 20% on anti-depressants. Forty-eight patients received BoNT injections and returned for follow-up. Six patients did not follow-up due to problems with transportation. Fifty-five control participants, group matched for age and gender, were included. Nine percent of controls were on benzodiazepines and 11% on anti-depressants.

Table 1
Cervical dystonia (CD) versus controls.

	CD[a] ($n = 54$)	Controls[a] ($n = 55$)	p[b]
Age (years)	62 (10.1)	62 (10.3)	>0.05
Gender (female)	80%	81%	>0.05
PSQI	7.50 (4.2)	4.25 (2.6)	<0.0005
ESS	5.04 (4.0)	3.96 (2.6)	0.1
BDI	9.30 (8.1)	3.13 (4.3)	<0.0005
HAM-A	7.93 (6.7)	3.44 (3.5)	<0.0005

PSQI – Pittsburg Sleep Quality Index; ESS – Epworth Sleepiness Scale; BDI – Beck Depression Inventory-II; HAM-A – Hamilton Anxiety Rating Scale.
[a] Values listed are Mean (SD).
[b] p values were calculated using the independent samples t test.

At baseline 65% of CD patients were defined as poor sleepers by PSQI > 5 compared to 31% of age-, and gender- matched controls. In CD patients sleep quality was impaired both at baseline (mean 7.50 (SD 4.2)) and follow-up (mean 7.46 (SD 4.3)). The mean PSQI score in controls was 4.25 (SD 2.6), which fell below the threshold for poor sleep (see Table 1). Direct comparison between the two groups showed worse quality of sleep in CD patients ($t = 4.82$, $p < 0.0005$). Compared to controls, CD patients exhibited more impairment in sleep disturbances ($p < 0.0005$), daytime dysfunction ($p < 0.0005$), sleep quality ($p < 0.0005$), sleep latency ($p = 0.008$), and habitual sleep efficiency ($p = 0.012$). Excessive daytime sleepiness, as measured by the ESS, was not significantly different between CD patients (mean 5.04 (SD 4.0)) and controls (mean 3.96 (SD 2.6)) ($t = 1.67$, $p = 0.1$) (see Table 1).

There was not a significant change in sleep quality ($t = 0.834$, $p = 0.41$) or excessive daytime sleepiness ($t = 1.77$, $p = 0.083$) in CD patients from baseline to follow-up, at peak of BoNT effect. This lack of change occurred despite a clear motoric benefit with BoNT treatment, as evidenced by the improvement in total TWSTRS from baseline (mean 32.93 (SD 9.2)) to follow-up (27.49 (SD 10.6)) ($t = 4.77$, $p < 0.0005$). All three subscales, including motor severity ($t = 4.49$, $p < 0.0005$), disability ($t = 3.33$, $p = 0.002$), and pain ($t = 3.18$, $p = 0.003$) improved with BoNT treatment (see Table 2).

Depressive symptoms were more common in CD patients (mean 9.30 (SD 8.1) compared to controls (mean 3.13 (SD 4.3)

Table 2
Pre- and post-botulinum toxin treatment.

	CD patients ($n = 48$)		
	Baseline[a]	Follow-up[a]	Mean difference
PSQI	7.50 (4.2)	7.46 (4.3)	0.04
ESS	5.04 (4.0)	4.60 (3.8)	0.44
TWSTRS	32.93 (9.2)	27.49 (10.6)	5.44[c]
Severity	17.32 (3.8)	15.41 (4.7)	1.91[c]
Disability	8.68 (3.7)	7.20 (4.0)	1.48[b]
Pain	6.93 (5.2)	4.88 (5.3)	2.05[b]
CDIP-58	123.75 (42.1)	115.16 (47.6)	8.59[b]
BDI	9.30 (8.1)	9.04 (8.7)	0.26
HAM-A	7.89 (6.7)	7.08 (5.9)	0.81

PSQI – Pittsburg Sleep Quality Index; ESS – Epworth Sleepiness Scale; TWSTRS – Toronto Western Spasmodic Torticollis Rating Scale; CDIP-58 – Cervical Dystonia Impact Profile; BDI – Beck Depression Inventory-II; HAM-A – Hamilton Anxiety Rating Scale.
[a] Values listed are Mean (SD).
[b] $p < 0.05$.
[c] $p < 0.0005$.

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