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ORIGINAL ARTICLE

Assessment of Non-Motor Symptoms in Cervical Dystonia

Esma Kobak Tur, Kadriye İrem Carus, Eren Gözke

Department of Neurology, University of Health Sciences Türkiye, Fatih Sultan Mehmet Training and Research Hospital, Istanbul, Türkiye

Abstract

Introduction: Cervical dystonia (CD) is a movement disorder characterized by cranial muscle overactivity, leading to an abnormal head posture. CD patients often experience mood disorders and sleep disorders due to the disturbing body image associated with deformities, and these symptoms can be at least as disabling as motor symptoms. This study investigated the frequency of non-motor symptoms and their relation to CD severity.

Methods: The study comprises 26 clients with CD and 26 healthy volunteers. The clinical severity of CD was assessed by the Toronto Western Spasmodic Torticollis Rating Scale. Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), Standardized Mini-Mental State Examination (SMMSE), Pittsburgh Sleep Quality Index (PSQI), and Epworth Sleepiness Scale were used to evaluate non-motor symptoms in patients with CD and healthy controls. All dystonia patients we included were receiving botulinum toxin therapy.

Results: The mean BDI and BAI scores were significantly higher in the patient group (p=0.006 and p=0.001, respectively). The mean score of SMMSE was considerably lower in the patient group than that in HCs (p=0.014). The frequency of excessive daytime sleepiness did not differ between groups. The patients with CD had worse sleep quality than HCs (p=0.001). According to the subgroup analysis of PSQI, sleep onset latency and sleep disturbance were significantly higher in the patient group (p=0.001 and p=0.012, respectively). Furthermore, sleep duration and sleep efficiency were significantly lower in the patient group (p=0.001 and p=0.001, respectively). No significant correlation was found between non-motor symptoms and disease severity, age, and duration of disease in the CD (p>0.05).

Discussion and Conclusion: CD causes functional impairment in many patients and leads to difficulties such as lack of self-confidence, timidity, avoidance of social movements, and depressive mood. Therefore, a comprehensive assessment of the non-motor symptoms of patients diagnosed with CD can also increase treatment success.

Keywords: Anxiety; cervical dystonia; depression; quality of life; sleep disturbances.

Dystonia could be a movement disorder typically characterized by maintained or episodic prolonged muscle contractions, inflicting twisting, repetitive movements, and abnormal postures. Dystonia usually originates from self-generated activities and is related to overflowing muscle activation[1].

The most common type of dystonia is cervical dystonia (CD), with a prevalence of 4.98/100 000. CD is characterized by overly active cranial muscle, resulting in an abnormally sustained head posture[2].

Although CD is outlined by its motor manifestations, there have additionally featured non-motor symptoms that con-

Correspondence: Esma Kobak Tur, M.D. Department of Neurology, University of Health Sciences, Fatih Sultan Mehmet Training and Research Hospital, Istanbul, Türkiye
Phone: +90 538 338 79 55 **E-mail:** esmakbk@hotmail.com
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siderably contribute to incapacity and reduce the quality of life[3-5]. Furthermore, anxiety, depression, poor sleep, excessive daytime sleepiness, and cognitive disturbances are notable non-motor manifestations that damage the standard of life in patients with CD[5].

The loops that reciprocally interconnect between basal ganglia with the cerebral cortex and cerebellum organize behavioral aspects, motor activity, saccadic eye movements, motivation, and executive function[5,6]. In dystonia, the most frequently basal ganglia, but occasionally parietal cortex, cerebellum, brainstem, and upper spinal cord functions are primarily affected, so it is known that the planning and the execution of both motor and cognitive functions within these behavioral domains have been destroyed[5,6].

Jahanshahi et al.[7] accentuated that depression in CD patients is characterized by impaired body image and low self-concerning, which is due to disfigurement caused by involuntary contraction of the head muscles. Similarly, in another study involving clients with CD, blepharospasm, and writer's cramp, depression and anxiety were reported as the most significant determinants of poor standard of life[4]. The stigma of CD patients due to their disability affects their emotional state, social life, and mental functions, as well as restricts their daily activities and physical processes[8].

In a prospective study investigating sleep quality in clients with CD, the researchers point out that, despite improving motor symptoms, sleep quality did not improve in patients with botulinum toxin therapy. This result showed that sleep disturbance in SD patients is an independent entity from motor symptoms[9].

According to our information today, there is no study on this subject in our country. We aim to designate the frequency of anxiety, depression, sleep disturbance, excessive daytime drowsiness, and cognitive decrease in our CD patients and to investigate the relationship of these non-motor symptoms with the severity of the disease and botulinum toxin treatment.

Materials and Methods

Participants

This research is a single-center cross-sectional clinical trial. It comprised 26 clients with CD, and 26 healthy volunteer acknowledged to the department of neurology at Fatih Sultan Mehmet Research and Training Hospital. A neurologist specializing in movement disorders evaluated the patients and diagnosed them based on the published criteria[10]. We excluded patients with a history of drug use, which may be the cause of dystonia, and patients with abnormal findings on conventional MRI. We eliminated patients with concomitant psychiatric disorders (such as depression and anxiety), other neurological abnormalities, or a family history of dystonia. We also excluded patients with genetic dystonia, those diagnosed with neurodegenerative diseases, and those who would not be able to understand the questions on the assessment forms.

We enclosed the healthy volunteers paired for sex, age, and duration of training with the patients. All participants were notified about the research and obtained their informed consent. The ethical committee of the University of Health Sciences, Fatih Sultan Mehmet Research and Training Hospital approved this study with approval number 2022/104. The study has been conducted in accordance with the Helsinki guidelines.

Clinical Evaluation of Patients with CD and Assessment of the NMSs

Face-to-face interviews were conducted with CD patients who were questioned for the duration of the disease, botulinum toxin unit, drug history, age, and sex. The Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) was used for the measurement of the clinical severity of CD[11]. All dystonia patients we included were receiving botulinum toxin therapy.

We used the Beck depression inventory (BDI) to determine the degree of depression. We asked the clients about their mood in the last week. The total scores range from 0 to 63. A value above ten on the BDI score demonstrates depression[12].

We assessed the degree of anxiety using a 21-item Beck Anxiety Inventory (BAI) scale[13]. A score of 0–21 showed low, a score of 22–35 showed moderate, and a score of 36 and above showed potentially concerning anxiety levels.

We assessed the sleep quality using the Pittsburgh Sleep Quality Index (PSQI)[14]. The PSQI scale consists of seven sleep areas: Sleep efficiency, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleeping pills, and daytime dysfunction. A value above 5 of PSQI shows poor sleep quality.

We used the Epworth Sleepiness Scale (ESS) to evaluate daytime drowsiness. A value above 10 indicates excessive daytime sleepiness[15].

Cognitive status was performed using the standardized mini–mental state examination (SMMTSE). A score of less than 23/24 on the SMMSE was defined as cognitive impairment[16].

Statistical Analysis

Number Cruncher Statistical System 2007 (Kaysville, Utah, USA) program was used to analyze all data. The descriptive statistical methods used to evaluate the study data are: mean, standard deviation, frequency, and rate. The Shapiro–Wilk Test was used to determine the distribution of the data. The Mann–Whitney U Test was used for the binary groups to compare the quantitative data. Spearman correlation analysis was used to evaluate the relationship between numerical variables. A $p<0.05$ was accepted for the significance level of the study data.

Results

We outlined the demographic and clinical characteristics of the subjects in Table 1. A comparison of the sex and age among the patient and the healthy control group showed no difference. In the patient group, the mean duration of disease was 9.85±6.39 years, the mean TWSTRS score was 12.42±4.21, and the mean botulinum toxin unit was 138.27±39.62. Among the CD patients, 14 (53.8%) suffered from depression, and 21 (80.7%) suffered from anxiety. The rate of depressed and anxious patients was significantly higher than healthy controls (HCs). Three patients (11.5%) suffered from cognitive deficits, and none of the HCs had cognitive deficits. In the patient group, cognitive impairment was significantly higher than in controls. Fifteen patients (57.6%) suffered from sleep disorders, and none of the HCs had sleep disorders. Sleep disorders were significantly higher in the patient group. Finally, excessive daytime drowsiness did not vary among groups.

Table 2 presents the frequency of each area of non-motor

Table 1. Characteristics of subjects and prevalence of NMSs among patients and controls

	Patient (n=26) Mean±SD (Median)	Control (n=26) Mean±SD (Median)	p
Age	49.96±13.8 (50)	48.69±11.3(48.5)	0.647
Sex (male/female)	6/20	5/21	0.500
Duration of disease(year)	9.85±6.39 (8)		
TWSTRSS	12.42±4.21 (12)		
Botulinum toxin (unit)	138.27±39.62 (137.5)		
Depression(yes/no)	14/12	4/22	0.004**
Anxiety (yes/no)	21/5	8/18	0.001**
Cognitive disorder (yes/no)	3/23	0/26	0.015*
Sleep disorder (yes/no)	15/11	0/26	0.001**
Excessive daytime Sleepiness (yes/no)	2/24	2/24	0.695

Chi-square test **p<0.01, *p<0.05, SD: Standard deviation, TWSTRSS: Toronto Western spasmodic torticollis rating scale-severity scale.

Table 2. Prevalence of each domain of NMS of included CD patients and matched HC

	Patient (n=26) Mean±SD (Median)	Control (n=26) Mean±SD (Median)	p
BDI	11.96±7.97 (10)	5.92±3.7 (6.5	0.006**
BAI	13.15±7.12 (12.5)	5.46±3.47 (4)	0.001**
ESS	3.62±3.46(3.5)	5.15±3.45 (4.5)	0.065
SMMSE	26.27±2.18 (26)	27.85±2.19 (28)	0.014*
PSQI global score	6.15±4.26 (5)	2.65±1.06 (3)	0.001**
PSQI sleep quality	1±0.75(1)	0.69±0.55 (1)	0.123
PSQI sleep oncet latency	1.46±1.1 (1)	0.35±0.63 (0)	0.001**
PSQI sleep duration	0.62±0.75 (0)	0.08±0.27 (0)	0.001**
PSQI sleep efficiency	0.65±0.69 (1)	0.08±0.27 (0)	0.001**
PSQI sleep disturbance	1.46±0.58 (1)	1.12±0.33 (1)	0.012*
PSQI hypnotic drugs	0.23±0.82 (0)	0.04±0.2 (0)	0.526
PSQI daytime dysfunction	0.73±1.15 (0)	0.31±0.74 (0)	0.116

Mann–Whitney U Testi *p<0.05 **p<0.01, BDI: Beck depression ınventory, BAI: Beck anxiety ınventory, ESS: Epworth sleepiness scale, SMMSE: Standardized mini-mental state examination, PSQI: Pittsburgh sleep quality index.

symptoms of included CD patients and healthy volunteers. The mean BDI score was 11.96±7.97, and also the mean BAI score was 13.15±7.12, considerably higher within the patient cluster (p=0.006 and p=0.001, respectively). The mean score of SMMSE was 26.27±2.18, significantly lower within the patient cluster than in HCs (p=0.014). The PSQI total score was 6.15±4.26 in the patients with CD, and it was considerably superior than in HCs (p=0.001).

In the patient cluster, sleep onset latency and sleep disturbance subgroups of PSQI were considerably higher compared to the controls (p=0.001 and p=0.012, respectively).

On the contrary, sleep duration and sleep efficiency of PSQI subgroups were considerably lower within the patient cluster (p=0.001 and p=0.001, respectively).

Finally, we could not detect any significant correlation between non-motor symptoms and illness severity, age, and duration of disease within the CD patients.

Discussion

We have determined that sleep disorders, neuropsychiatric symptoms, and cognitive impairment are quite widespread in Turkish CD patients.

We could not discover any relationship between non-motor manifestations and the clinical severity of CD. Excessive daytime drowsiness was not varied among the patients and healthy volunteers.

The elevated incidence of depression and anxiety discovered in our CD patients reminds the results of other studies[17-19]. In a recent study, the researchers included 289 CD patients and showed that the most substantial predictor factors affecting patients' standard of life were depression and anxiety[20]. Furthermore, Tomic et al.[8] emphasized increasing the degree of depression and anxiety affected the disability of CD patients. The pathologic process of depression and anxiety in patients with dystonia continues to be unclear. Nevertheless, many neurophysiological studies have demonstrated that corticostriatal-thalamocortical circuits contribute to psychiatric symptoms as well as motor symptoms[21,22]. Furthermore, neuroimaging studies related to depression detected structural abnormalities in brain regions involved in emotion regulation, such as the cingulate cortex, precuneus, prefrontal area, and thalamus[23].

One study showed that motor symptoms and pain improved with neurotoxin treatment within dystonia patients, but depression persisted[24]. Gündel et al.[18] indicated that the severity of depression in clients with dystonia is not correlated with the severity of dystonia and suggested a primary rather than a secondary abnormality. Another study, similar to our findings, found that depression and anxiety continue regardless of the severity of dystonia[25]. These findings indicate the existence of mood disorders in dystonia patients independently of the secondary conclusions, such as stigma and pain. Furthermore, the researchers showed that more than 50% of patients with dystonia experience depression before motor findings[26]. Moreover, mood disorders could also be the initial sign of this disease. Prospective disquisitions are required to discover the pathophysiological connection between mood disorders and dystonia.

Recent papers investigating sleep disorders in CD have shown an increased prevalence of sleep disturbances[9,25,27]. Factors that impact sleep quality in patients with CD include pain due to involuntary contractions, mood diseases, and drugs used to treat dystonia. Yang et al.[25] found that CD clients have bad sleep quality compared to blepharospasm clients, and they suggested low sleep quality related to pain which is a majority in CD but missing in blepharospasm. Another polysomnography study conducted with CD patients showed that electromyography (EMG) recordings with abnormal muscle activity decreased when patients lay on the bed before sleep. Subsequently, abnormal EMG activity disappeared in all dystonia patients during the transition from wakefulness to non-rapid eye movement sleep stages. Finally, they found the intensity and unpleasantness of cervical spine pain were reduced by about 50% during the night[28]. Two studies suggested sleep disorders in CD were partly due to the confounding effect of depression[27,29]. We used PSQI to evaluate the sleep quality in CD patients and could not find a relationship between dystonia severity and sleep quality. However, we found PSQI sleep onset latency and sleep disturbance to be noticeably high in our patient cluster; we thought that insomnia might be a comorbid disease in CD, similar to a previous study[27]. We evaluated daytime sleepiness using ESS. Degradation of sleep quality did not affect daytime drowsiness in our dystonia patients; also we could not detect any difference from healthy volunteers. Our findings were in line with the studies of Eichenseer and Avanzino et al.[9,27] In contrast to our study, Trotti et al.[30] found a high rate of daytime sleepiness in dystonia patients. They have established that medications, including anticholinergics and benzodiazepines frequently used to treat dystonia, can affect daytime drowsiness. One study investigated the effect of botulinum toxin treatment on the sleep quality of CD patients. They indicated that following botulinum toxin treatment had a durable betterment in the severity of CD but did not improve sleep quality[9]. Hence, sleep quality in the CD requires an individual assessment for effective

treatment. Sleep disorders should not be considered a secondary complication to the motor manifestations of CD.

This study found lower cognitive performance in CD clients compared to healthy volunteers. However, the limitation of our research is that we did not conduct a detailed neurocognitive assessment. Maggi et al.[31] showed a selective deficit in time-based prospective memory in focal dystonia, previous corroborating evidence of cognitive dysfunctions in dystonic patients. Romano et al.[32] demonstrated that clients with cranial-CD might have impairment in specific cognitive areas associated with processing speed, working memory, and visual motor ability. According to the study of Jahanshahi et al.[33] unlike other movement disorders associated with frontostriatal dysfunction, for instance, Parkinson's disease or Huntington's disease, CD was not related to deficits in the tests of executive function or working memory used. However, this study was conducted on only ten patients.

The shortcoming of this study was its small sample size and cross-sectional study. We could not determine the causal connection between motor severity and non-motor symptoms of CD patients. In addition, we did not perform a more detailed neuropsychological examination in our study group. This study did not investigate other non-motor manifestations such as pain and fatigue. However, to the best of our information, this is the initial study investigating non-motor findings with CD patients in our country.

Conclusion

Even if the motor symptoms of the patients are treated, the concomitant sleep, mood, and cognitive disorders can negatively affect the quality of life if they are not diagnosed and interfered with instantly. It may cause functional dysfunction in several clients and cause difficulties, for instance, lack of confidence, timidity, dodging of social activities, and depressive mood. Therefore, judging the patient by perceptive the non-motor functions of the patients diagnosed with CD is crucial.

Ethics Committee Approval: University of Health Sciences, Fatih Sultan Mehmet Research and Training Hospital Ethics Committee approved the study (Decision number: 2022/104, Date: September 08, 2022).

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