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COMORBIDITY OF NEUROPATHY OF MEDIAN AND ULNAR NERVES IN PARKINSON'S DISEASE PATIENTS

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ABSTRACT

Objective: The aim of this article is to find the neuropathy of ulnar and median nerves in Parkinson's disease patient. Subjects: Fifty subjects were enrolled in this study. They were classified into group (I): 25 patients had Parkinson's disease and group (II) constitutes 25 normal healthy individuals used as controls. **Methods:** All patients and control subjects were subjected to electrophysiology parameters of median and ulnar nerves that were recorded and statistically compared. **Results:** According to electrophysiology, we confirmed median neuropathy in 8 patients (16.0%); bilateral in 5 patients and unilateral in 3 patients and ulnar neuropathy in 4 patients (8.0%) of the PD group. While mean age (p = 0.0021), age at PD onset (p = 0.0081), and H&Y scores (p = 0.0122) were significant, tremor and rigidity scores were not. **Conclusion:** Medial and ulnar neuropathy was observed in PD patients and a disease related peripheral neurodegeneration beyond symptom severity occurs.

KEYWORDS: Parkinson's disease, Neuropathy, median, ulnar.

INTRODUCTION

Parkinson's disease (PD) is a common degenerative disease of central nervous system among middle-aged populations. Characterized by distal resting tremor, rigidity, bradykinesia, and postural disturbances. Patients with PD may have sensory dysfunctions such as visual dysfunction, olfactory dysfunction, vestibular dysfunction, furthermore pain. Most of these dysfunctions are relatively little from a clinical point of view but can be more easily demonstrated through electrophysiological or psycho-physical tests.[1]

Diagnosis of parkinson's disease is mainly depends on the history taking, symptoms, and physical examination, which are difficult to be measure and to be objective. Hence there are a variable symptoms and severity of PD, the clinical staging of PD cannot be accurately measured in clinical practice. The peripheral neuropathy (PN) may be due to the defect in nerve cell body, axons or myelin sheath and it results in decreased nerve conduction velocities and amplitudes in peripheral nerves. The most commonly involved nerves are the ulnar and median nerves, as the distal and sensory nerves are affected earlier. Carpal tunnel syndrome is the main cause of peripheral nerve damage due to median nerve entrapment[2] (Gupta et al., 2016). The characteristic rest tremor seen as "pillrolling" action of the hands has been also accused of being the trigger of the carpal tunnel syndrome because of causing repetitive trauma to the median nerve.[3]

Although the pathogenic mechanism remains unclear, some studies suggest PN as a neurodegenerative process involving both central and peripheral nervous systems.[4]

Electrophysiology (EP) is a commonly used non-invasive technique for objective diagnosis of the functional changes in neural conductive pathway of PD. Some studies demonstrated Sensory nerve conduction velocity (SNCV) and motor nerve conduction velocity (MNCV) in patients with PD, but the results were inconsistent.[5,6]

So, our study explored the ulnar and median neuropathy in patients with Parkinson's disease.

PATIENTS AND METHODS

Fifty persons were enrolled in this study. They were recruited from outpatient clinic of both Neurology Departments, at Saudi German Hospital, KSA since Jan 2016 till Jan 2017, in corporation with Neurology Department New Damitta-Al-Azhar University, Egypt. The study protocol was approved by The Local Ethical Committee, parents of enrolled patients signed written

fully informed consent for study participation and undergoing the assigned investigations.

The fifty patients were classified into two equal groups each of 25 persons. Group I (patient's group): comprised 25 patients proved to have Parkinson's disease, while group II (control group): comprised 25 normal individuals who have no pathological disease affecting the wrist. All of the study groups had been examined by neurologists and had fulfilled the study criteria according to the following.

Inclusion criteria: 1. Patients had no other systemic and/or local manifestations of any other disease affecting the wrist (ulnar or median nerve). 2. Patients had to be able to make informed consent whether verbal or written to make legal consent before starting the study.

Exclusion criteria: included coexistence of any systemic disease known to cause median or ulnar neuropathy such as diabetes mellitus, chronic renal failure, hypothyroidism, rheumatoid arthritis, cervical radiculopathy, and elbow or wrist trauma (previous fractures of the wrist or elbow were excluded).

All patients and control groups were subjected to the following:

Personal Data
Age, sex, occupation (present or previous), residence… etc

History
- Previous PD full history.
- History of previous neurological conditions.
- History of any systemic and autoimmune diseases.
- History of drug intake especially in chronic diseases.

Clinical examination
General examination: including pulse, temperature, blood pressure, thyroid, lymph nodes.

Neurological examination: All patients were examined in the "on" condition by means of the United Kingdom Parkinson's Disease Society Brain Bank Clinical DiagnosisCriteria.[7] The Hoehn and Yahr (H&Y) disability scale[8] and Unified Parkinson's Disease Rated Scale (UPDRS)[9] were used to assess the severity of the disease. The patients were not symptomatic regarding pain or numbness suggesting nerve entrapment in the territory of a root or nerve.

Patients were examined for existence of any median or ulnar neuropathy according to the electrophysiologically diagnostic criteria based on control data performed in the laboratory.

As known, PD symptoms begin unilateral initially and in the following years the initial affected extremities demonstrate more severe symptoms when compared with the latter affected ones. Keeping this rule in mind, we compared the initial and latter affected sides of each patient electrophysiologically in regard to tremor and rigidity severity.

In elderly subjects, subclinical neuropathy is common and might increase the frequency of mono-neuropathy. Electrophysiological indices of the patients were compared to the means of and the controls for any statistically significant difference also. Later, each patient was categorized as mild or severe according to the H&Y scores, tremor and rigidity severity, and disease duration. These groups electrophysiologic parameters were compared statistically.

As regard the control group, no history of frequent, repetitive use of the hand, wrist, or elbow, and no trauma or any other condition affecting peripheral neural transmission and whose neurologic examination was normal were included in the study. The subjects were volunteers from the community matched by age and sex with the PD patients. Any subject with electrophysiological pathology was excluded from the study.

Informed consent was obtained from all individual participants included in the study and the study was approved by the Ethical Committee of Mansoura Faculty Medicine, Mansoura University, Egypt.

Electrophysiological Evaluation
Sensory nerve conduction velocity (SNCV) and motor nerve conduction velocity (MNCV) were measured with a Medelec Synergy Electromyography instrument (Oxford Instruments Medical, Inc., UK) in an air-conditioned room at 23 ^{o}C to 25 ^{o}C. Limb temperature was maintained above 32 ^{o}C using a warm compress if needed during the nerve conduction studies. Median and ulnar nerve conduction studies were performed bilaterally in all patients and control groups utilizing the standard technique of supra-maximal percutaneous stimulation.[10]

The EMG finding criteria for diagnosis of median nerve neuropathic affection include prolonged distal motor latencies of the median nerve greater than 4.2 m/s, a decrease in sensory conduction velocity below 41 m/s for digit-wrist segment, 5 mV for amplitude of muscle action potential, and 10 mV for amplitude of sensory nerve action potential.[10]

The EMG criteria for diagnosis of ulnar neuropathy include prolonged motor nerve conduction velocity (NCV) from above elbow (AE) to below elbow (BE) of less than 40 m/s and an AE to BE segment greater than 10 m/s slower than BE to wrist (W) segment which suggests conduction block or temporal dispersion indicative of focal demyelination.

Statistical Analysis

Data were collected, tabulated and presented as mean ± standard deviation (X ± SD) or median range as minimum & maximum. Categorical variables were presented by frequency and percentage. Comparisons between two categorical variables were performed using the Chi-square analysis. Kruskal-Wallis test or one-way ANOVA (analysis of variance) were used for comparison of more than two independent samples followed by the Bonferroni-adjusted Mann–Whitney *U* test. All analyses were performed using the SPSS medical statistics version 21 (IBM, Armonk, NY USA). All tests were two-sided and a *p* value of less than 0.05 was considered to be statistically significant, while p value of more than 0.05 were considered statistically insignificant. A *p* value of less than 0.01 was considered statistically highly significant and p value of less than 0.001 was considered statistically very highly significant.

RESULTS

All patients receiving treatment for Parkinson's disease were examined during the "on" condition. The clinical characteristics of the study population are summarized in table (1).

According to diagnostic electrophysiologic criteria of the patients' group (I), 14 wrists (28.0%) in 10 patients (20.0%) were diagnosed as having definite median neuropathy and 5 elbows (10.0%) in 3 patients (6.0%) were diagnosed as having ulnar neuropathy. The electrophysiologic parameters of the healthy control group (II) were in normal limits.

Table 1: Clinical characteristics of the patients and the control group.

Variables	Patient group	Control group	Total
Males No. (%)	15 (30%)	13 (26%)	28 (56%)
Females No. (%)	10 (20%)	12 (24%)	22 (44%)
Mean age (years)	*70.2 ± 12.6	*69.8 ± 11.9	70.5 ± 12.25
Mean age of onset (years)	61.8 ± 11.2		
PD duration (years)	7.31 ± 4.22		
H&Y stage	2.92 ± 0.84		
UPDRS part III score	22.74 ± 9.13		
PD questionnaire	66.61 ± 25.8		

* p = 0.213 between patients and control groups.

The clinical characteristics of the patients with median neuropathy are listed in Table (2).

Table 2: Demographic and clinical characteristics of PD patients with median neuropathy versus without median neuropathy.

Variables	Median neuropathy (+)	Median neuropathy (−)	p value
Mean age	79.3 ± 3.12	63.4 ± 11.3	0.0021*
PD duration (year)	8.59 ± 3.26	6.31 ± 3.41	0.3131
Age at PD onset	69.2 ± 4.22	59.5 ± 10.9	0.0081*
Tremor score	2.39 ± 1.01	1.66 ± 0.82	0.2825
Rigidity score	2.61 ± 0.51	1.86 ± 0.88	0.0618
H&Y stage	3.82 ± 1.16	2.84 ± 0.93	0.0122*
UPDRS part III score	32.46 ± 12.7	21.36 ± 10.3	0.0451*
PD questionnaire	88.61 ± 14.5	55.62 ± 13.5	0.0084*

* p <0.05

Median neuropathy was diagnosed as bilateral in 5 patients (10.0%) and unilateral in 3 patients (6.0%). Among the patients with median neuropathy, mean age (p = 0.0021), age at Parkinson disease onset (p = 0.081), Hoehn and Yahr stage (p = 0.0122), UPDRS III motor score (p = 0.00451), and Parkinson disease questionnaire scores (p = 0.0084) were statistically significantly higher. Parkinson disease duration (p = 0.3131), Tremor score (p = 0.2825) and rigidity score (p = 0.0618) were statistically non-significantly different.

Ulnar neuropathy in this study was observed in 4 patients (8%) represented in table (3).

Table 3: Demographic and clinical characteristics of PD patients with ulnar nerve neuropathy versus without ulnar nerve neuropathy.

Variables	Ulnar neuropathy (+)	Ulnar neuropathy (−)	*p value*
Mean age	78.8 ± 2.98	61.6 ± 10.6	0.0019*
PD duration (year)	6.96 ± 2.22	5.23 ± 3.14	0.2833
Age at PD onset	67.3 ± 4.01	55.8 ± 9.27	0.0091*
Tremor score	2.13 ± 0.89	1.05 ± 0.74	0.5221
Rigidity score	2.14 ± 0.66	1.64 ± 0.48	0.0584
H&Y stage	3.12 ± 1.08	2.42 ± 0.67	0.0092*
UPDRS part III score	30.5 ± 11.9	19.8 ± 9.33	0.0315*
PD questionnaire	82.5 ± 12.4	51.12 ± 11.9	0.0068*

* p <0.05

Ulnar neuropathy was diagnosed as bilateral in 4 patients (8.0%) and unilateral in 1 patient (2.0%). Among the patients with ulnar neuropathy, mean age (p = 0.0019), age at Parkinson disease onset (p = 0.091), Hoehn and Yahr stage (p = 0.0092), UPDRS III motor score (p = 0.0315), and Parkinson disease questionnaire scores (p = 0.0068) were statistically significantly higher. Parkinson disease duration (p = 0.2833), Tremor score (p = 0.5221) and rigidity score (p = 0.0584) were statistically non-significantly different.

The comparison of the means of electrophysiological indices on the left and right sides between controls and the patients is shown in Table (4).

Table 4: The mean indices of electrophysiologic parameters between PD patients and controls.

Electrophysiologic parameters	PD group	Control group	*p value*
R median digit 2 velocity (s)	52.7 ± 3.56	57.3 ± 8.34	0.0398*
L median digit 2 velocity (s)	51.9 ± 4.06	56.9 ± 7.48	0.0294*
R ulnar digit 5 wrist velocity (s)	57.4 ± 5.16	55.8 ± 9.39	0.2162
L ulnar digit 5 wrist velocity (s)	54.3 ± 5.62	56.2 ± 4.44	0.0412*
R median APB wrist latency (m)	3.82 ± 1.05	3.21 ± 0.58	0.0185*
R median APB wrist amp. (m)	6.82 ± 2.26	8.98 ± 2.23	0.0401*
R median APB elbow latency (m)	7.47 ± 0.84	5.74 ± 1.08	0.0212*
R median APB elbow amp. (m)	4.95 ± 2.27	7.41 ± 2.19	0.0134*
R median APB elbow velocity (m)	58.1 ± 6.44	64.3 ± 7.54	0.0095*
L median APB wrist latency (m)	4.85 ± 0.39	3.05 ± 0.28	0.0001*
L median APB wrist amp. (m)	6.67 ± 2.61	7.16 ± 2.05	0.0928
L median APB elbow latency (m)	8.72 ± 2.01	6.88 ± 1.08	0.0065*

L median APB elbow amp. (m)	6.09 ± 2.11	6.46 ± 2.06	0.2622
L median APB elbow velocity (m)	60.2 ± 10.5	64.8 ± 12.6	0.0821
R ulnar ADM wrist latency (m)	2.86 ± 1.01	2.33 ± 0.91	0.0187*
R ulnar ADM wrist amp. (m)	9.42 ± 1.45	9.59 ± 1.61	0.4455
R ulnar ADMb.elbow velocity (m)	61.7 ± 3.44	62.2 ± 3.81	0.1667
R ulnar ADMa.elbow velocity (m)	59.8 ± 3.21	58.9 ± 1.64	0.1845
L ulnar ADM wrist latency (m)	3.65 ± 0.95	2.28 ± 0.84	0.0111*
L ulnar ADM wrist amp. (m)	10.4 ± 1.12	10.1 ± 1.09	0.4648
L ulnar ADMb.elbow velocity (m)	57.9 ± 3.33	64.1 ± 4.08	0.0014*
L ulnar ADMa.elbow velocity (m)	53.5 ± 2.99	58.2 ± 3.18	0.0171*

(s): sensorial; (m): motor; R: right; L: left; amp: amplitude; APB: abductor pollicis brevis; ADM: adductor digiti minimi; a: after; b: below.

Table 5: Correspondence of mean indices of electrophysiologic parameters between initial and later symptomatic sides in PD patients.

Electrophysiologic parameters	Initial symptomatic side	Later symptomatic side	*p value*
Median digit 2 latency (s)	2.87 ± 0.06	2.76 ± 0.09	0.3866
Median digit 2 velocity (s)	51.9 ± 3.86	48.8 ± 4.97	0.0197*
Median digit 2 peak amp. (s)	37.8 ± 9.65	36.7 ± 9.31	0.3662
Ulnar digit 5 wrist latency (s)	2.54 ± 0.14	2.17 ± 0.12	0.4232
Ulnar digit 5 wrist velocity (s)	53.8 ± 3.25	53.1 ± 2.08	0.1887
Ulnar digit 5 wrist peak amp. (s)	30.3 ± 12.6	29.9 ± 12.2	0.6886
Ulnar latency (m)	25.7 ± 10.4	20.1 ± 9.81	0.0628
Median latency (m)	2.95 ± 0.27	2.88 ± 0.19	0.8834
Median peak amp. (m)	22.1 ± 8.41	20.3 ± 7.55	0.2295
Median APB wrist latency (m)	3.89 ± 1.32	3.95 ± 1.08	0.4651
Median APB wrist amp. (m)	6.67 ± 2.31	6.11 ± 2.02	0.1981
Median APB elbow latency (m)	8.72 ± 1.01	8.18 ± 0.58	0.6234
Median APB elbow amp. (m)	6.09 ± 2.11	5.96 ± 2.16	0.4602
Median APB elbow velocity (m)	59.2 ± 6.15	61.8 ± 5.62	0.2501
Ulnar ADM wrist latency (m)	2.86 ± 0.91	2.73 ± 0.74	0.7877
Ulnar ADM wrist amp. (m)	9.42 ± 1.45	10.9 ± 1.61	0.1525
Ulnar ADMb.elbow latency (m)	6.72 ± 0.64	6.82 ± 0.86	0.6657
Ulnar ADMb.elbow amp. (m)	9.08 ± 2.21	8.99 ± 1.96	0.2855
Ulnar ADMb.elbow velocity (m)	61.5 ± 7.95	61.8 ± 6.48	0.7123
Ulnar ADMa.elbow latency (m)	7.86 ± 1.02	7.92 ± 1.92	0.4768

Ulnar ADMa.elbow amp. (m)	8.94 ± 2.13	8.91 ± 2.08	0.8655
Ulnar ADMa.elbow velocity (m)	55.5 ± 4.99	56.2 ± 5.18	0.7599

(s): sensorial; (m): motor; R: right; L: left; amp: amplitude; APB: abductor pollicis brevis; ADM: adductor digiti minimi; a: after; b: below.

Table 6: The statistical comparison of mean indices of median and ulnar nerve electro physiologic parameters at the wrist level between mild and severe patient groups and controls.

Variables	Disease duration (years)		Hoehn & Yahr score		Rigidity		Tremor	
	Shorter than 6 years	Longer than 6 years	Mild	Severe	Mild	Severe	Mild	Severe
m-dml								
R	NS	0.002	0.032	NS	0.006	NS	0.004	0.004
L	NS	0.001	0.013	0.001	0.002	0.001	0.003	NS
m-amp								
R	NS	NS	NS	0.044	NS	NS	NS	NS
L	NS	NS	NS	NS	NS	NS	NS	NS
m-ncv								
R	NS	NS	NS	0.035	NS	NS	NS	NS
L	NS	NS	NS	NS	NS	NS	NS	NS
u-dml								
R	NS	0.028	NS	NS	NS	0.036	NS	NS
L	NS	0.007	NS	0.025	0.032	NS	NS	0.012
u-amp								
R	0.029	0.032	NS	NS	NS	NS	NS	NS
L	NS	NS	NS	NS	NS	NS	NS	NS
u-ncv								
R	NS	NS	NS	NS	NS	NS	NS	NS
L	NS	NS	NS	NS	NS	NS	NS	NS

m: median; dml: distal motor latency; amp: amplitude; ncv: nerve conduction velocity; u: ulnar; NS: not significant; R: right; L: left.

While right and left median nerve sensorial velocities at the wrist were decreased, right and left median nerve motor latencies were prolonged statistically significantly indicating demyelination. There was a significant decrease in the right median nerve motor amplitude whereas the decrease in the left median nerve motor amplitude did not reach statistically significant levels. It might be suggested that there was a possible median nerve axonal deterioration also. While there was a significant decrease in the left ulnar nerve sensorial velocity at the wrist, the decrease in the right ulnar nerve did not reach significant level. The prolongation of the right and left ulnar nerves' motor latencies were significant. These findings suggested ulnar nerve demyelination at the wrist when compared with the age-gender matched controls. The reduction in the left ulnar nerve motor velocity at the elbow level was significantly decreased while the reduction in the right was not significant. These results suggested a tendency to ulnar nerve entrapment at the elbow in the patient group.

In concordance with our hypothesis that more severe tremor and rigidity might worsen neuronal transmission, we compared each patient's median and ulnar nerve electrophysiology parameters between the initial and latter affected extremities (Table 5). All parameters regarding ulnar and median nerves were studied and mean indices were compared with each other. No significant difference was found but if we could have learned the time span between the first and second affected sides of the body for each patient accurately and categorized it as years, the results might have been more objective.

Later, each patient was categorized as mild or severe according to the mentioned criteria; Mild H&Y (Hoehn & Yahr) group (stage I-II) including 10 patients (20%) with an age group range of 48–78 years (mean age 69.8 ± 11.9) and the severe H&Y group (stage III-IV) including 15 patients (30%) with an age group of 46–84 years (mean age 70.2 ± 12.6, p = 0.213). In this study, the mean of disease duration was calculated as 7.31 ±

4.22 years statistically, and mild group suffering from the disease for 6 years or less consisted of 9 patients (18%) with an age group range of 48–77 years (mean age 64.1 ± 10.9) and the severe group with more than 6 years of the disease consisted of 12 patients (24%) with an age group range of 49–84 years (mean age 66.8 ± 11.6, p = 0.122); mild tremor group (score 0-1-2) consisted of 16 patients (32%) with an age group range of 48–79 years (mean age 65.1 ± 10.1) and the severe tremor group (score 3-4) consisted of 5 patients (10%) with an age group range of 59–83 years (mean age 72.2 ± 9.85, p = 0.1771); mild rigidity group (score 0-1-2) consisted of 15 patients (30%) with an age range of 48–81 years (mean age 68.5±9.89) and the severe group consisted of 6 patients (12%) with an age group range of 54–81 years (mean age 71.56 ± 10.1, p = 0.121).

In our study population, the statistical evaluation of the median of the duration of the disease as years was calculated as "6" years. The median and ulnar motor latencies at the wrist of the patients who had been suffering from the disease for more than 6 years were found to be significantly prolonged bilaterally.

According to the Hoehn and Yahr scores, bilateral median nerve motor latencies were found to be prolonged at the wrist significantly in the mild group (Table 6) suggesting a tendency to demyelination.

According to the rigidity and tremor scores, bilateral median nerve motor latencies at the wrist were found to be prolonged (Table 6) only in the mild group but not in the severe group.

There was no significant difference in ulnar nerve electrophysiologic parameters at the elbow level in the patient group neither regarding initial and latter affected sides nor regarding mild and severe groups and disease duration.

DISCUSSION

Whatever thought for contribution of the peripheral nervous system in P D We should have to consider concomitant disorder in those patients. The prevalence of peripheral neuropathy in the general population is about 2.4% overall, however this might be increase to as high as 8% in elderly persons, with diabetes mellitus which appear to be the commonest predisposition. So, this high prevalence should be considered in any population, especially an elderly patient. The estimated prevalence of IPD is 0.1-0.2% of the general population, also this increased to 1% of those patients above 60 years of age.[11] So, a small number of patients may have concomitant and unrelated Parkinsonism and peripheral neuropathic affection which may be estimated to be less than 0.01% of those elderly above 60 years of age if based on chance alone.[12]

In this study, we found the frequency of cubital tunnel syndrome (CTS) is significantly prominent in older and more severe patients. Most of the results of CTS were bilateral. Ratios mentioned above were significantly higher, calling attention to median neuropathy in PD. Similarly, Yucel et al.[13] found frequency of CTS as 24.4% electrophysiologically in their study where they reported a larger median nerve cross-sectional area sonographically in the severe PD patients. The anatomical site, wrist, was also evaluated in PD patients sonographically by Yang et al.[3] and median nerve cross-sectional area indicating median nerve swelling with edema was found to be larger in concordance with tremor severity due to the cumulative injury. This study is in coordination with the study of Yardimci et al.[14] who stated that although CTS was more prominent in patients suffering more severe disease, tremor and rigidity were not found to be contributing factors to median neuropathy evolution.

Rigidity, defined as a hypertonic state with increased resistance within the range of movement about a joint,[15] may lead to tendon contractures and atrophy[16] and trigger the characteristic limb posture called striatal deformity accompanied by flexion at the elbow, ulnar deviation at the wrist, flexion at the metacarpophalangeal joints, and extension at the interphalangeal joints in varying severity.[8] Moreover, repetitive movement of the elbow superimposed by rest tremor at the wrist causes a narrowing of the tunnel and constriction of the nerve initiating a cycle of inflammation and edema and increases the strain. The cubital tunnel cross-sectional area narrows as intraneural pressures increase up to 20-fold.[17]

We found that ulnar neuropathy was present in 6% of the PD group electrophysiologically, this was inconsistent with Yardimci et al.[14] who found 3.22% in PD group with ulnar neuropathy whereas the incidence of the ulnar neuropathy (cubital tunnel syndrome) in the general population has been reported as 24.7 per 100.000.[18] However, Yardimci et al.[14] did not find any association between neither rigidity and tremor severity nor H&Y scores and disease duration and ulnar neuropathy existence.

Axonal neuropathy causing decreased amplitude values whereas loose myelin causes prolonged distal motor latency and decreased sensorial nerve conduction velocities electrophysiologically in the peripheral nerves.[19] In the patient group, we evaluated significant median and ulnar demyelination at the wrist bilaterally and a tendency to ulnar nerve entrapment at the elbow being significant at the left and probable at the right. Advancing age factor in the development of entrapment neuropathy was excluded in the study population.

In this study, there was a relationship between median and ulnar nerve demyelination with both mild tremor and rigidity groups and mild H&Y group. As Parkinson's disease is progressive, mild symptomatology in the above mentioned groups confirms that these patients are

at the early stages of the disease. Evidence suggests that peripheral nervous system involvement, sometimes occurring before clinical diagnosis, might be discussed as an intrinsic peripheral neuropathy before spreading of neurodegeneration to the central nervous system (CNS).[2] Moreover, neuronal loss due to alpha-synuclein deposition, impaired axonal transport, and mitochondrial dysfunction causing neuronal death in the brain is being discussed as pathomechanisms of the neurodegenerative process in PD.[14]

Our results indicating no association with tremor and rigidity severity and mononeuropathy evolution are in accordance with the findings that in each individual PD patient suffering from different tremor and rigidity severity asymmetrically no difference was found in median and ulnar nerve neural transmission electrophysiologically. This is in association with Yardimci et al.[14] where they excluded the extrinsic factors such as levodopa medication and intrinsic factors such as disease duration in each patient and had the opportunity to focus on symptom severity and asymmetry only.

In chronic demyelinating neuropathies, neuropathic tremor was reported in antagonist muscle pairs with a frequency of 3 to 6 Hz which is similar to rest tremor. It has been proposed that distortion of the peripheral sensory input and feedback to the CNS, as the result of demyelination, leads to mismatch in spindle and tendon organ afferents and errors in the timing of muscle activity generated within the CNS.[20] The tremor is most dominant in the upper extremities. As evaluated in our study, the demyelination of median and ulnar nerves especially at the wrist level might be an additive factor for tremor generation in the hands.[14]

Yardimci et al.[14] observed median and ulnar demyelination at the wrist level in patients suffering from the disease for a longer period. The patients with longer disease duration were not older than the ones with a shorter disease period. In our study population, the mean of disease duration was calculated as 6 years statistically. In the literature, peripheral neuropathy with the advanced disease is mostly related with cumulative levodopa intake.[2]

Future studies must be done on larger scale populations to overcome the limitation of this study. Other studies must support the hypothesis that severity of rigidity and tremor might contribute to mononeuropathy evolution and investigate symptom severity regarding tremor and rigidity as a potential risk for mononeuropathy generation in each individual patient which provide a better understanding of the disease and will guide the clinician while applying patient specific therapeutic options in PD.

In conclusion, according to the results of this study, PD causes peripheral neuropathy of ulnar and median nerves which draw an attention to disease related intrinsic factors in peripheral neuro-degeneration.

AUTHORS' CONTRIBUTIONS

This work was carried out in collaboration between three authors. Authors O.A. designed the study and wrote the protocol. Author Z.A. preformed the statistical analysis, managed the literature search and wrote the first draft of the manuscript with assistance from author M.A. All authors shared in collection of patients, read and approved the final manuscript.

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