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Electrodiagnostic Features of Ulnar Nerve in Patients with Chronic Obstructive Pulmonary Disease

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Abstract

Background & Objectives: Present study was aimed to assess abnormalities of ulnar nerve in stable COPD patients.

Method: Study comprised of 60 healthy adults and 60 stable COPD patients (40-50 years) with no clinical neuropathy. Duration of illness and spirometric indices (FEV1%, FEV1/FVC, PEFR %) were assessed. Nerve conduction study of motor and sensory component of ulnar nerve was recorded bilaterally using RMS EMG MKII. Distal latency, nerve conduction velocity and compound motor action potential (CMAP) and sensory nerve action potential (SNAP) were analysed. Significant abnormality was defined as variations beyond mean ± 2SD from healthy adults.

Results: Observations revealed significantly prolonged distal latency and decreased conduction velocity (demyelination), decreased CMAP (axonal loss) bilaterally of both sensory and motor components of ulnar nerve in COPD patients compared with controls.

Interpretation & conclusion: Observation suggests that hypoxemia of COPD, by inducing direct action on nerve fibres or pontomedullary portion of brain or by enhancing effect of other neurotoxic substances causes nerve impairment.

Keywords: *Nerve conduction study, hypoxemia, demyelination, axonal loss.*

Introduction

Chronic obstructive pulmonary disease (COPD) is a common preventable and treatable disease, characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases[1]. COPD has been identified to have multisystem involvement with significant extrapulmonary manifestations. Patients with COPD frequently suffer from various comorbidities, such as cardiovascular disease, osteoporosis, depression, malnutrition, metabolic syndrome, diabetes, and lung cancer. These comorbidities have a major impact on quality of life and survival. The mechanisms by which the many COPD-related comorbidities develop are still unclear. It has been suggested that systemic inflammation also contributes to the disease process. In spite of this, its causes are likely multifactorial (inactivity, poor diet, hypoxia, and inflammation). [2]

Smoking, long lasting COPD, airway obstruction is believed to affect ponto medullary portion of brain by altering blood gases causing hypoxemia, hypercapnia and respiratory acidosis [3]. Association of COPD patients with peripheral neuropathy has been reported in previous studies. [4, 5] The association of polyneuropathy with COPD is described in literature [6-12]

Hypoxemia is the most important cause[13]. Hypoxia results from hyperventilation and ventilation perfusion imbalance. There is restrictive transport of oxygen in

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COPD as a result of reduced partial oxygen tension. The dependence of peripheral nerve tissue on oxygen was established. Hypoxemia causes harmful effect to the vaso nervosum and thus peripheral nerve damage results[14]. While electrophysiological studies in COPD usually reveal a sensorial type neuropathy mostly in the distal parts of the extremities, in severe cases the neuropathy may be characterized by loss of axons which may sometimes be also accompanied by demyelination.[15]

With this background the study was undertaken to evaluate electrodiagnostic changes in ulnar nerve in COPD patients and to correlate these changes with severity of disease.

Material and Method

The study was conducted in Department of Physiology in collaboration with Department of Pulmonary Medicine and was approved by the institutional ethical comittee. Based on the sample size calculated[16] 60 COPD cases, who fulfilled the inclusion and exclusion criteria and were willing to participate in the study were selected and compared with healthy volunteers willing to be investigated to serve as controls for electrophysiological study. Duration of illness ranged from 2 to 5 years.

There was no evidence of diabetes, prediagnosed neuropathy in these subjects on clinical examination, and detailed history. Blood pressure of all the cases were in normotensive range. On spirometric investigation FEV1/FVC was more than 70%. All participants were informed about the study and written consent was obtained.

Spirometric tests were done by using RMS–Helios 401 spirometer and the best of three consecutive tests was taken into consideration. Certain drugs used by COPD patients were restricted for a period as advised by the treating physician. Forced Vital Capacity (FVC), Forced expiratory volume in 1 second (FEV_1), the ratio of FEV_1/FVC, peak expiratory flow rate (PEFR), forced expiratory flow during the middle half of FVC (FEF 25-75) were measured. Pre and Post bronchodilator study was done in all COPD cases. Post Bronchodilator response was marked by significant irreversibility in COPD. Nerve conduction study of ulnar nerve (motor and sensory) was done using RMS EMG MAK II. Distal latency (DL), nerve conduction velocity (NCV), compound motor action potential (CMAP) and sensory nerve action potential (SNAP) were recorded.

Cases with reduced CMAP and SNAP were classified as axonopathy and increased distal latency and/or reduced conduction velocity were classified under demyelinating neuropathy. Cases in which all the parameters were altered were classified as mixed (axonal and demyelinating both) neuropathy.

Normal parameters of ulnar nerve are as follows[17]

Nerve	DL	CMAP (mV)	MNCV (m/s)
Ulnar motor nerve	2.19-2.99 (ms)	6.48-10.54	55.72-67.18
Ulnar sensory nerve	2.43-3.23 (μV)	3.17-7.91	48.07-60.27

For ulnar motor nerve conduction study[17, 18]

A supramaximal stimulation keeping the cathode close to the active recording electrode was given. The arm was positioned in a 45-degree abducted and externally rotated posture with elbow flexed to 90 degrees and the forearm in neutral position.

Sensitivity: 5 mV/division

Sweep speed: 5 ms/division

Low cut filter: 2 Hz

High cut filter: 5 KHz

Stimulus: 20-30 mA

The surface recording electrodes were placed in belly tendon montage, keeping the active electrode close to the motor point (hypothenar eminence, halfway between the level of the pisiform bone and the 5th metacarpophalangeal joint) and reference to the tendon (slightly distal to the 5th metacarpo phalangeal joint).

Ground electrode was placed between stimulating and recording electrodes at the dorsum of the hand.

A biphasic action potential with initial negativity is thus recorded.

Ulnar Nerve sensory nerve conduction[17, 18]

A subminimal stimulation keeping the cathode close to the active recording electrode was given

Sensitivity: 20 μV /division

Sweep speed: 2 ms /division

Low cut filter: 20 Hz

High cut filter: 3 KHz

Stimulus: 8-10 mA

In the supine/sitting position active ring electrode (A) was placed in contact with the radial and ulnar sides of the 5th digit, slightly distal to the base of the digit and reference electrode (R) was placed 4 cm distal to the active electrode (or in small fingers as far distally as possible). Ground electrode (G) was on the dorsum of the hand. Subject was asked to straighten the fingers and stimulation was given slightly radial to the tendon of flexor carpi ulnaris.

Statistical Analysis: All values were expressed as Mean ± Standard deviation. Student t test was used to compare groups. Statistical analysis was done using SPSS-16.0.

Result

Table 1: Spirometric indices of controls and COPD patients

Parameters	Controls (n=60)	COPD Patients (n=60)	t	p
FEV_1 (% predicted)	95.97 ± 34.21	53.58 ± 26.45	7.59	0.0001
FEV_1/FVC (%)	88.88 ± 11.07	52.92 ± 11.3	17.6	0.0001
FVC (% predicted)	92.53 ± 24.34	73.38 ± 20.57	4.65	0.0001
PEFR (% predicted)	88.7 ± 39.6	45 ± 18.97	7.7	0.0001

Post bronchodilator irreversibility (<12%)

All the respiratory parameters of COPD patients were found to be significantly decreased as compared to control groups. FEV1/FVC was <70% in all COPD patient.

Table-2: Comparison of Motor and Sensory Ulnar Nerve Conduction Parameters of Control and Study Group

Nerve	Electrophysiological variables	Control group (n=60)		COPD group (n=60)		t	p
		Right I	Left II	Right III	Left IV	I vs III II vs IV	
Ulnar (motor)	Distal latency (ms)	2.15 ± 1.49	1.6 ± 0.47	2.24 ± 0.96	2.62 ±1.04	0.39 6.9	NS 0.0001
	CMAP (mV)	7.57 ± 1.49	6.9 ± 0.51	5.81 ± 1.57	5.99 ±1.73	6.29 3.92	0.0001 0.0001
	MNCV (m/s)	54.96 ±5.53	53.91± 3.91	48.97 ± 6.1	50.37±8.41	5.63 2.95	0.0001 0.0038
Ulnar (sensory)	Distal latency (msec)	1.94±0.63	1.81±0.64	2.01±0.5	2.35±0.87	0.67 3.87	NS 0.0002
	SNAP (μV)	26.7±9.19	21.33±4.02	20.04±9.6	26.38±18.58	3.88 -	0.0002 -
	SNCV (m/s)	54.66 ±5.45	55.06±5.39	53.32±11.85	56.7±19.46	0.79 -	NS -

Significantly Prolonged Distal Latency of Left Ulnar nerve, Reduced CMAP and Reduced conduction velocity of both Right and Left Ulnar motor nerve was seen in COPD group as compared to controls.

An attempt was made to compare Sensory Nerve Conduction parameters of the control group and COPD group. Electrophysiological variables recorded showed prolonged Distal Latency in COPD cases as compared to controls in Left Ulnar sensory nerve.

Significantly decreased SNAP was found in Right ulnar sensory nerve in COPD group as compared to controls.

Table 3: Distribution of Peripheral Neuropathy in Ulnar Nerve (n=60)

Motor Nerves	Axonal	Demyelinating	Mixed
LT Ulnar Motor	7	20	22
RT Ulnar Motor	3	17	28
RT Ulnar Sensory	6	12	06
LT Ulnar Sensory	15	09	10

Mixed type of peripheral neuropathy was predominant in Ulnar motor nerve (Right Ulnar 46.6% and Left Ulnar 36.6% cases)

Left Ulnar sensory nerve showed axonal degeneration in 25% of cases

Discussion

COPD has many important systemic effects during natural course of disease secondary to multiple factors such as systemic inflammation, oxidative stress, and hypoxemia. Many authors have reported abnormalities in ulnar nerve in COPD patients. [19, 20]

Studies in the past have suggested the existence of impaired peripheral nerve functions in patients with COPD, though the prevalence of peripheral neuropathy have markedly varied from one study to another. The difference in the prevalence of neuropathy reported might be attributable to number of nerves studied in few studies only two nerves, one sensory and one motor[8, 19], three nerves[6] or different nerves[13, 7] were investigated. In the present study ulnar motor and sensory nerves of both right and left limb were tested. Chronic respiratory insufficiency has been implicated as one of the factors for peripheral neuropathy [20-22].

Hypoxia, tobacco smoke, alcoholism, malnutrition and certain drugs are believed to be the etiopathogenic factor. Hypoxia probably is the most common cause of peripheral neuropathy affecting nerve fibres either directly or by enhancing the effects of other neurotoxic factors or deficiencies[22].

In the present study distal latency was significantly increased, and amplitude and conduction velocity was significantly decreased of left ulnar motor nerve comparative to increased distal latency of left ulnar sensory nerve. Similar findings were present in right ulnar nerve. Amplitude and conduction velocity was significantly reduced of right ulnar motor nerve compared to reduced amplitude of the sensory component.

Above findings are suggestive of mixed neuropathy in ulnar motor nerve bilaterally and demyelinating and axonal neuropathy of left and right ulnar sensory nerve respectively. Slowing of conduction velocity of motor nerves was also reported by other authors[19]

Prevalence of neuropathy was more predominant in left ulnar nerve both sensory (56.6%) and motor (80%) component compared to 40% and 25% of right ulnar sensory and motor nerve respectively in our study.

Pfeiffer G et al[8] (1990) associated polyneuropathy and chronic hypoxemia and studied prevalence of neuropathy in patients with COPD. 13 patients out of 43 had only electrophysiological abnormalities.

They correlated rate and severity of the neuropathy with severity of chronic hypoxemia, PaO2 and age

Narayan and Ferranti[19] (1978) reported three times greater incidence of ulnar abnormalities in 90% patients of COPD. Chronic hypoxemia was believed as the cause of peripheral neuropathy.

Faden et al[7] (1981) associated subclinical neuropathy in patients with chronic obstructive pulmonary disease. Slowing of sensory and motor conduction in 87% of cases suggesting demyelination was reported.

El-Shinnawya (2017)[23] evaluated ulnar and median nerves by means of electrophysiological nerve study. Ulnar nerve motor neuropathy was proved in 36% of patients, there was an increase in DL, decrease in motor nerve conduction velocity, and longer F-wave latency in the COPD group than in the control group in both nerves. They reported demyelinating ulnar motor neuropathy similar to our study also.

Marandi M et al (2015) reported significant difference of sensory left ulnar nerve amplitude with COPD severity[24]. Kazi K et al (2014) and Demir R et al (2014) reported involvement of ulnar nerve in COPD patients[25-26]. Reduced amplitude suggestive of axonal degeneration was reported by these authors.

Agrawal D et al (2007)[27] in their study on subclinical peripheral neuropathy in stable middle-aged patients with chronic obstructive pulmonary disease reported peripheral nerve impairment in 5 out of 30 COPD patients on electrophysiological evaluation. Significantly reduced amplitude in ulnar nerve with predominantly sensory axonal polyneuropathy compared with healthy controls was reported.

The presumed etiopathogenic factors are chronic hypoxia, smoking and duration of disease playing either direct action on nerve fibers or Ponto-medullary portion of brain or by enhancing the effect of other neurotoxic substances cause impairment of nerves involved. High carboxyhaemoglobin level in smokers is believed to be one of the cause of peripheral neuropathy. Slowing of nerve conduction has been correlated to amount of smoking in various studies[7, 19, 15]. It has been suggested that nicotine when taken on long term basis, may be toxic to peripheral nerves[7].

Improvement in peripheral nerve function has been noted in some patients following treatment of malnutrition, suggesting metabolic abnormalities in schwann cell or malnutrition as a probable cause of peripheral neuropathy[6].

Thus early identification of the peripheral neuropathy in COPD patients with no clinically detected impairment may help in planning and management of the COPD patients.

Conclusion

The observation of the study revealed mixed neuropathy in ulnar motor nerve bilaterally and demyelinating and axonal neuropathy of left and right ulnar sensory nerve respectively suggesting that hypoxia caused by airway obstruction in COPD may cause abnormality in peripheral nerve characterised by loss of axons and degeneration of schwann cells resulting in axonopathy or demyelination. Findings from this study indicate that peripheral neuropathy occurred in association with mild chronic respiratory insufficiency.

Study limitation: No investigation of the blood gas levels in COPD patients is the limitation of the study.

Conflict of Interest: None

Source of Funding: None

Ethical Clearance: taken by Institutional Ethical Committee

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