National Journal of Physiology, Pharmacy and Pharmacology

RESEARCH ARTICLE

Nerve conduction study of median nerve with severity of airway obstruction

Sanjeev Kumar Shrivastava[1], Rashmi Dave[1], Asha Shrivastava[2]

[1]Department of Physiology, Gandhi Medical College, Bhopal, Madhya Pradesh, India, [2]Department of Physiology, Chirayu Medical College, Bhopal, Madhya Pradesh, India

Correspondence to: Rashmi Dave, E-mail: rdave1987@gmail.com

Received: March 06, 2019; **Accepted:** March 28, 2019

ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is frequently associated with significant extrapulmonary manifestations. Hypoxemia resulting in peripheral neuropathy is known to occur as a systemic manifestation of COPD. **Aims and Objectives:** This study aims to analyze the abnormalities of sensory and motor component of median nerve in stable COPD patients and correlate the changes with severity of COPD, duration of disease, and pack-years. **Materials and Methods:** The study comprised 60 stable COPD patients (40–50 years) with no clinical neuropathy. Duration of illness, pack-years, and spirometric indices (forced expiratory volume in 1 s % [FEV1%], FEV1/forced vital capacity, and peak expiratory flow rate %) were assessed. Electrodiagnostic study of the right and left median nerve was done using root mean square EMG MKII. Distal latency, nerve conduction velocity, and action potential (compound motor action potential [CMAP] and sensory nerve action potential [SNAP]) for median motor and sensory nerve were analyzed. COPD patients were classified on the basis of the level of airway obstruction (FEV1 >50% and FEV1< 50%) into two groups and correlation of electrodiagnostic variables of these two groups with duration of illness, pack-years, and level of airway obstruction was established. **Results:** CMAP of the left median motor nerve was reduced with increasing severity of disease. Significant correlation was established with spirometric variables, quantum of smoking, and duration of illness. **Conclusion:** Airway obstruction leads to changes in arterial blood gas analysis (hypoxemia, hypercapnia, and acidosis) resulting in impairment of nerve conduction.

KEY WORDS: Chronic Obstructive Pulmonary Disease; Hypoxemia; Demyelination

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease characterized by airflow limitation which is usually progressive and is associated with an abnormal inflammatory response of the lungs to noxious particles or gases, primarily caused by cigarette smoking. It also produces significant systemic consequences.[1]

Access this article online	
Website: www.njppp.com	Quick Response code
DOI: 10.5455/njppp.2019.9.0311328032019	

Genetic and environmental factors are responsible risk factors of this multifactorial disease. The interplay of these factors is important in the development of COPD. The major site of increased resistance in COPD is small airways and alveolar sacs resulting in airway obstruction. Metaplastic goblet cells, replacement of with and infiltration of mononuclear inflammatory cells, and mucus-secreting cells by replacing surfactant secreting Clara cells smooth muscle hypertrophy and excess mucus, edema, and cellular infiltration[2] cause luminal narrowing. Airflow limitation, the major physiologic change in COPD, can result from both small airway

obstruction and destruction of gas-exchanging air spaces, i.e., the respiratory bronchiole, alveolar ducts, and alveoli.

Destruction of lung tissue occurs due to increase in proliferation of the structural cells along with increased apoptotic alveolar epithelial (vascular endothelial cell growth factor, caspase-3, and ceramide) and endothelial cells result in and the development of emphysema, pro-inflammatory chemokines, and cytokines into the circulation marks the development of extrapulmonary manifestation. Excess amount of leukocytes, C-reactive protein, interleukin (IL)-6, IL-8, fibrinogen, and tumor necrosis factor is released into the circulation, leading to persistent low-grade inflammation.[3]

Hypoxia results from hyperventilation and ventilation-perfusion imbalance. Reduced partial oxygen tension causes restrictive transport of oxygen in COPD. Hypoxemia causes harmful effect to the vaso nervosum affecting cell body, axon, Schwann cells, connective tissue, or vascular supply resulting in peripheral nerve damage.[4,5] Histologic and electrophysiologic characteristics indicated the presence of peripheral nerve disorders resulting in subclinical peripheral neuropathies.[5,6]

COPD begins with complex biochemical and cellular events in the small airways and surrounding alveoli resulting in loss of elastic recoil. The lungs begin to increase in size and the forced vital capacity [FVC] increases.[7]

The airway lumen is reduced due to mural inflammation of small airways and airways remodeling. Thus, combination of airways inflammation and remodeling, bronchospasm, mucous hypersecretion, and loss of elastic recoil cause inflammation of small airways and airways remodeling.[8] Forced expiratory volume in 1 s (FEV1)/FVC of <70% heralds the onset of rapid declines in FEV1 over the course of a 10-year period.[7]

Table 1: Normal parameters of median nerve

Nerve	DL (ms)	CMAP	MNCV (m/s)
Median motor	3.37–4.17	5.48–10.72 mV	54.76–62.28
Median sensory	2.65–3.47	4.43–13.39 μV	36.05–54.85

DL: Distal latency, CMAP: Compound motor action potential, MNCV: Motor nerve conduction velocity

While electrophysiological studies in COPD in the past usually reveal a sensory type of neuropathy mostly in the distal parts of the extremities, it is characterized by loss of axons which may sometimes be also accompanied by demyelination in severe cases.[9]

As this disease runs a stable course for long duration and associated comorbidities are usually present in late stages, early diagnosis of the symptoms by electrodiagnostic study may help in reducing comorbidities associated with the disease and improving the quality of life of COPD patients.

MATERIALS AND METHODS

The present study was conducted in the Department of Physiology, Gandhi Medical College, Bhopal, in collaboration with the Department of TB and Chest Medicine and was approved by the institutional ethical committee (Approval no. 14593-94/MC/7/2014). 60 stable COPD patients who fulfilled the inclusion and exclusion criteria, willing to participate were selected for the study and the participants were divided into two subgroups on the basis of FEV1 >50% and FEV1 <50%. Severity of COPD was assessed according to the level of airway obstruction. In each subgroup, 30 patients were chosen. The COPD patients were either current smokers (76.6%) or non-smokers (23.3%). Smoking pack-years were calculated using Dr N J Masters and Catherine Tutt smoking pack-year calculator.[10]

Inclusion Criteria

The following criteria were included in the study:

- Clinically stable COPD patients in the age range of 40–50 years.
- No known endocrinal, metabolic, renal, cardiovascular (CV) disorder, pre-diagnosed neuropathy, and resting blood pressure <140/90 mmHg.

Exclusion Criteria

The following criteria were excluded from the study:

- Very severe grade of COPD patients with comorbidities.
- Patients with asthma, recent myocardial infarction or unstable angina, endocrinal, and metabolic or renal disorder.

Table 2: Relevant characteristics of the study population

Variables	Group I FEV1>50% predicted (*n*=30)	Group II FEV1<50% predicted (*n*=30)	*t*	*P*
Pack-years	25.03±21.4	34.3±28.3	1.43	NS
Duration of illness	5.63±3.63	16.33±4.48	10.1	0.0001
FEV1 (% predicted)	76.4±17.5	30.76±6.16	13.4	0.0001
FEV1/FVC (%)	57.57±9.52	47.96±10.71	3.6	0.0005
FVC (% predicted)	88.26±16.37	58.50±11.40	8.1	0.0001
PEFR(% predicted)	54.06±19.23	35.93±13.85	4.1	0.0001

PEFR: Peak expiratory flow rate, FEV1: Forced expiratory volume in 1 s %, FVC: Forced vital capacity, *Post-bronchodilator irreversibility (<12%), *COPD patients were classified as Group I and Group II on the basis of % FEV1 predicted (>50% and <50%, respectively), COPD: Chronic obstructive pulmonary disease

- History of neurotoxic drugs or pre-diagnosed peripheral neuropathy.

Spirometric tests were done using root mean square [RMS] – Helios 401 spirometer. FVC, forced expiratory volume in 1 s (FEV1), the ratio of FEV1/FVC, peak expiratory flow rate, and 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.

Nerve conduction study of median 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. Abnormal parameters were classified under three types of neuropathy.

- Reduced CMAP/SNAP – axonopathy.
- Increased DL and/or reduced NCV – demyelinating neuropathy.
- Reduced CMAP/SNAP and increased DL and/or reduced NCV – mixed neuropathy.

Normal parameters of median nerve are as follows.[11]

Median Motor Nerve Conduction Study[11]

In the supine/sitting position, a supramaximal stimulation keeping the cathode close to the active recording electrode was given Table 1.

- Sensitivity: 5 mV/division
- Sweep speed: 5 ms/division
- Low cut filter: 2 Hz
- High cut filter: 5 KHz
- Stimulus: 20–30 mA

Active electrode (A): Between the midpoint of the distal wrist crease and the first metacarpophalangeal joint. Reference electrode (R): Distal to the first metacarpophalangeal joint. Ground electrode (G): On the dorsum of the hand. Stimulation point (S1): 8 cm proximal to the active electrode and (S2): Slightly medial to the brachial artery pulse in the antecubital region.

Median Sensory Nerve Conduction[11]

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: 6–10 mA

Active electrode (A): A ring electrode was placed in contact with the radial and ulnar sides of the 2nd digit being tested, slightly distal to the base of the digit. Reference electrode (R): 4 cm distal to the active electrode. Ground electrode (G): The dorsum of the hand. Stimulation point: Over the median nerve at the wrist, between the tendons of flexor carpi radialis and palmaris longus or medial to flexor carpi radialis tendon.

Table 3: Changes in nerve conduction study parameters of motor and sensory nerves with increasing severity of disease

Nerve	Group I (*n*=30)	Group II (*n*=30)	*t*	*p*
Right median motor				
DL	2.6±0.7	2.8±0.5	1.27	NS
Amplitude	9.0±2.7	8.2±0.7	1.57	NS
Left median motor				
DL	2.8±0.7	3.01±0.9	1.00	NS
Amplitude	8.8±2.1	7.5±2.2	2.34	0.02
Conduction velocity	52.3±4.5	51.7±5.3	0.47	NS
Right median sensory				
DL	2.4±0.7	2.6±0.8	1.03	NS
Amplitude	33.2±12.3	32.2±16.4	0.26	NS
Left median sensory				
DL	2.2±0.4	2.4±0.3	2.19	NS
Amplitude	31.4±16.6	27.1±17.4	0.97	NS
Conduction velocity	61.6±14.7	56.8±13.6	1.31	NS

DL: Distal latency

Table 4: Relation of airway obstruction and peripheral neuropathy of median nerves in COPD group

Nerves	Group I	Group II
Right median motor	9	5
Left median motor	2	13
Right median sensory	3	5
Left median sensory	6	11

*FEV1 >50%, **FEV1 <50%, COPD: Chronic obstructive pulmonary, FEV1: Forced expiratory volume in 1 s %

Statistical Analysis

All values were expressed as mean ± standard deviation. Student's *t*-test was used to compare groups. Bivariate correlations between variables were evaluated by Pearson's correlation. Statistical analysis was done using the Statistical Package for the Social Sciences-16.0.

RESULTS

Quantum of smoking as measured by pack-years was statistically insignificant in two groups ($P > 0.05$) Table 2. All the spirometric indices (FEV1, FEV1/FVC, FVC, and peak expiratory flow rate [PEFR]) in two subgroups of COPD patients were significantly reduced ($P < 0.05$) in Group II than Group I Table 3.

On comparing electrodiagnostic variables of median motor and sensory nerves, CMAP of the left median nerve was

Table 5: Correlation of electrophysiological indices of Group I with spirometric variables, quantum of smoking, and duration of illness

Nerve	FEV1%	FEV1/FVC	Pack-years	Duration
Right median motor				
DL	−0.01	0.13	0.12	+0.37
Amplitude	+0.35	+0.51	−0.08	−0.28
Conduction velocity	−0.23	−0.08	−0.08	0.23
Left median motor				
DL	−0.01	0.01	0.40	0.01
Amplitude	0.12	−0.01	−0.09	−0.01
Conduction velocity	−0.15	−0.14	0.15	−0.14
Right median sensory				
DL	−0.10	−0.29	−0.12	−0.08
Amplitude	+0.40	+0.39	0.11	−0.35
Conduction velocity	−0.13	+0.05	−0.02	0.39
Left median sensory				
DL	0.09	+0.41	−0.01	0.13
Amplitude	0.00	0.06	0.21	−0.20
Conduction velocity	−0.12	−0.21	0.19	−0.06

*P<0.05 for r>0.349 (significant), DL: Distal latency, FEV1: Forced expiratory volume in 1 s %, FVC: Forced vital capacity, COPD: Chronic obstructive pulmonary disease

Table 6: Correlation of nerve conduction study parameters of Group II with FEV1, FEV1/FVC, pack-years, and duration of illness

Nerve	FEV1%	FEV1/FVC	Pack-years	Duration
Right median motor				
DL	−0.01	0.00	−0.11	0.37*
Amplitude	−0.13	−0.27	0.20	0.34
Conduction velocity	0.54*	0.23	−0.37*	−0.42*
Left median motor				
DL	−0.22	0.02	−0.10	−0.10
Amplitude	−0.11	−0.15	−0.49*	0.05
Conduction velocity	0.02	0.18	−0.20	0.35
Right median sensory				
DL	−0.33	−0.14	0.05	0.42*
Amplitude	−0.08	−0.11	0.27	0.17
Conduction velocity	−0.12	0.10	−0.22	0.06
Left median sensory				
DL	−0.54	−0.01	0.00	0.30
Amplitude	−0.07	−0.29	0.14	0.06
Conduction velocity	0.52*	−0.05	−0.19	−0.39*

*P<0.05, DL: Distal latency, FEV1: Forced expiratory volume in 1 s %, FVC: Forced vital capacity, COPD: Chronic obstructive pulmonary disease

significantly reduced (P < 0.05) of COPD Group II as compared to Group I Table 4.

Neuropathy was present in 43.3% of cases and 33.3% of cases in motor and sensory left median nerve (more number of cases was involved in Group II). The presence of neuropathy in Group I can explain the neuropathic changes even in the early stage of disease Table 5 and 6.

Positive correlation of amplitude with FEV1 and FEV1/FVC and negative correlation of CV with FEV1 of the right median motor nerve were found significant.

A significant positive correlation of DL of the left median motor nerve with pack-years was established. Similar correlation of amplitude of the right median sensory nerve along with the duration of illness was seen. DL and FEV1/FVC were significantly positively correlated in the left median sensory nerve. Positive correlation of DL with the duration of disease was established in motor and sensory component of the right median nerve. Significant reduction in conduction velocity with reduced FEV1, smoking, and duration of illness was established in the right median motor nerve. Decrease in amplitude with increased pack-years was seen in the left median motor nerve. Significant positive correlation of conduction velocity with FEV1% and negative correlation with the duration of disease of the left median sensory was established.

DISCUSSION

Chronic respiratory insufficiency has been implicated as one of the factors for peripheral neuropathy.

In the present study, significant reduction in CMAP was present in the left median nerve in Group II COPD patients as compared to Group I suggestive of axonal loss with increasing severity of disease. In cases with increased airway obstruction, more number of median sensory nerves and left median nerve was involved. Abnormal electrodiagnostic parameters were also seen in other nerves in cases with FEV1 <50%, suggesting the involvement of neuropathy in the early stage of COPD. Neuropathy was present in more number of cases in the left median motor and sensory nerve as compared to the right median nerve. Of 60 COPD cases studied, neuropathy (either demyelinating or axonal) was detected in 25% and 29% of cases in the left median motor and sensory nerves. Involvement of neuropathy was also seen in Group I, suggesting that axonal loss or demyelination begins in the early course of disease which may be present subclinically, remains undiagnosed or may be presentable with symptoms such as tingling, numbness, or weakness of limbs. An attempt was made to correlate DL, CMAP, and SNAP and conduction velocity of median nerve (sensory and motor) with spirometric variables (FEV1 and FEV1/FVC), smoking, and duration of illness. It was established that in Group I with gradual reduction in FEV1 and FEV1/FVC, compound muscle action potential was also reduced in the right median nerve, thus establishing a positive correlation between nerve axonal damage and airway obstruction. Inverse correlation of amplitude with the duration of disease and of conduction velocity with FEV1 was significant in the right median sensory and motor nerve, respectively. Demyelinating changes were significantly correlated with pack-years and FEV1/FVC, respectively, of motor and sensory component of median nerve, respectively.

Narayan and Ferranti[12] reported 3 times greater incidence of median motor in 90% of COPD patients. Predominantly, sensory axonal neuropathy was also reported by Agrawal *et al*.[13] Hypoxemia and nerve ischemia lead to axonal degeneration, affecting large myelinated fibers first followed by smaller myelinated and unmyelinated axons may cause axonal damage in COPD.[12] Demyelination begins with penetration of macrophages at basal lamina of Schwann cells causing retraction of myelin at internodal junctions. Macrophages penetrate basal lamina of Schwann cells at internodes. Finger-like macrophage processes then enters between layers of myelin and peel them off. Myelin ovoids form and myelin is engulfed by macrophages. Satiated macrophages rapidly leave through bloodstream and leave behind Schwann cells with varying amounts of myelin and frequent bare axons resulting in demyelination.[14] Ulubay *et al*.[15] studied the effects of peripheral neuropathy on exercise capacity and quality of life in patients with COPD and identified mild axonal sensorimotor neuropathy in 53% of cases. They reported that FEV1 values were significantly lower in those who had peripheral neuropathy than those without. No significant correlation was detected between peripheral neuropathy development and age, BMI, smoking, and PFT parameters. COPD patients with neuropathy were having longer duration of illness, more pack-years, and severe airflow obstruction (FEV1 and PEFR) when compared to COPD patients with no neuropathy as reported by Agrawal *et al*.[13] Feki *et al*.[16] reported neuropathy in 17.50% and established positive correlation with smoking, duration of COPD, and pO2. Similar to our study, Asal *et al*.[17] reported demyelinating median motor neuropathy and established positive correlation with smoking, age, and FEV1.

Advancing age, cigarette smoking, and environmental pollution are considered to be the risk factors of COPD resulting in hypoxemia, which is supposed to be the most important factor responsible for neuropathy. History of smoking, duration of study, and all spirometric variables were recorded and correlated, but no investigation of the blood gas levels was done in our study.

CONCLUSION

The study concluded abnormal median nerve conduction parameters in both the early and late stages of disease suggest that there is a need of electrodiagnostic investigation in COPD. Correlation of neuropathy with smoking, duration of disease, and spirometric variables again emphasizes that mass ignorance of disease symptoms during early stages of disease precipitates severe irreversible systemic manifestation; thus, early diagnosis and treatment of COPD may help to prevent the agony, thus improving quality of life of the patient.

REFERENCES

1. European Respiratory Society. ERS ATS COPD Guidelines European Respiratory Society; 2005.

2. Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, *et al*. Harrison's Textbook of Internal Medicine. 17th ed., Vol. 2. New York: McGraw-Hill Professional Hardcover; 2008. p. 1638-39.
3. Tkac J, Man SF, Sin DD. Systemic consequences of COPD. Ther Adv Respir Dis 2007;1:47-59.
4. Kayachan O, Beder S, Deda G, Karnak D. Neurophysiological changes in COPD patients with chronic respiratory insufficiency. Acta Neurol Belg 2001;101:160-5.
5. Johnson PC, Asbury AK. The pathology of peripheral nerve. Muscle Nerve 1980;3:519-28.
6. Kaeser HE, Lambert EH. Nerve function studies in experimental polyneuritis. Electroenceph Clin Neurophysiol 1962; Suppl 22:29-35.
7. Petty TL, Silvers GW, Stanford RE. Mild emphysema is associated with reduced elastic recoil and increased lung size, but not with airflow obstruction. Am Rev Respir Dis 1987;136:867-71.
8. Burrows B, Earle RH. Course and prognosis of chronic obstructive lung disease. A prospective study of 200 patients. N Engl J Med 1969;280:397-404.
9. Sipahiolu B, Kzltan M, Hachekimolu A. COPD and neuropathy. Solunum 1995;19:960-6.
10. Roberts NJ, Evans G, Blenkhorn P, Partridge MR. Nigel Masters. Catherine Tutt: NHS Atlas of Variation in Healthcare for People with Respiratory Disease; 2010.
11. Misra K, Kalita J. Clinical neurophysiology. Indian J Med Res 2014;142:779.
12. Narayan M, Ferranti R. Nerve conduction impairment in patients with respiratory insufficiency and severe chronic hypoxemia. Arch Phys Med Rehab 1978;59:188-92.
13. Agrawal D, Vohra R, Gupta PP, Sood S. Subclinical peripheral neuropathy in stable middle-aged patients with chronic pulmonary pulmonary disease. Singapore Med J 2007;48:887.
14. Dahlin LB, Neckling LE, Lundstrom R, Lundborg G. Vibration exposure and conditioning lesion effect in nerves: An experimental study in rats. J Hand Surg 1992;17:858-61.
15. Ulubay G, Ulasli S, Bozbas S, Ozdemirel T, Karatas M. Effects of peripheral neuropathy on exercise capacity and quality of life in patients with chronic obstructive pulmonary diseases. Arch Med Sci 2012;2:296-302.
16. Feki W, Ketata W, Hammami I, Bahloul N, Rekik WK, Ayadi H, *et al*. Peripheral neuropathy in chronic obstructive pulmonary disease. Eur Respir J 2014;44.
17. Asal G, Cakan A, Erbaycu AE, Dereli S, Ozsoz A, Edipoglu H, *et al*. Electromyographic evaluation of peripheral nerves in chronic obstructive pulmonary disease. Turk Respir J 2003;4:51-6.

How to cite this article: Shrivastava SK, Dave R, Shrivastava A. Nerve conduction study of median nerve with severity of airway obstruction. Natl J Physiol Pharm Pharmacol 2019;9(6):534-539.

Source of Support: Nil, **Conflict of Interest:** None declared.