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A cross-sectional study on nerve conduction velocity in stable chronic obstructive pulmonary disease

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ABSTRACT

Objectives: This study was undertaken with the aim to find out possible presence of subclinical peripheral neuropathy in patients of chronic obstructive pulmonary disease (COPD) and its association with advancing severity of disease. Changes in nerve conduction parameter values in these patients have been presented.

Materials and Methods: Median, ulnar, peroneal motor, and sural sensory nerve conduction latency, amplitude, and velocity were recorded in 100 known cases of COPD in the age group of 25–65 years as per the standard protocol.

Results: On analysis, statistically significant lowering of sural nerve conduction velocity ($P = 0.002$) and amplitude ($P = 0.003$) was found with decreasing FEV1% in the three stages of COPD. Decrease in ulnar sensory conduction amplitude and velocity was also noted but it was not significant. Fall in sural nerve conduction velocity was found to be strongly and positively correlated ($P = 0.029$, r = 0.444) with decrease in FEV1%.

Conclusion: These findings suggest that with increasing severity of disease, airflow limitation enhances polyneuropathy in COPD patients. It is predominantly axonal and mainly involving sensory nerve.

Keywords: Nerve conduction velocity, Chronic obstructive pulmonary disease, Peripheral neuropathy, Subclinical neuropathy

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a disorder characterized by expiratory airflow limitation that is not fully reversible. Parenchymal destruction and emphysematous disease are often associated with many patients of COPD.[1] In 2005, COPD was the cause for 7% deaths and 3% disability-adjusted life years lost in India.[2]

COPD also leads to many important systemic effects such as skeletal muscle dysfunction, anemia, nutritional abnormalities, cardiovascular, and neurological disorders[3] which have been attributed to multiple factors such as systemic inflammation, oxidative stress, and hypoxemia.[4]

Prevalence rate of peripheral neuropathy (PNP) in patients suffering with COPD has been stated between 28% and 94% in the literatures with smoking, chronic hypoxia, malnutrition, age, drugs, and metabolic derangement proposed as the possible causes.[5]

Nerve conduction study is a highly specific and non-invasive technique used to differentiate between an axonal and demyelinating neuropathy. It also contributes to establish the extent and distribution of the lesion.[6]

The purpose of the study is to use this modality of testing to establish a possible relationship between the stages of COPD categorized on forced expiratory volume (FEV) at the end of first second (which is a measure of severity of chronic disease) and PNP seen in these patients.

MATERIALS AND METHODS

The study was conducted in the Department of Physiology in collaboration with the Department of Pulmonary Medicine in Grant Government Medical College and Sir J.J. Group of Hospital in Mumbai with prior permission of ethical committee. Diagnosis of COPD was done on the basis of history of cough, sputum production, and exertional dyspnea. General physical examination followed by respiratory system examination was done to detect for cyanosis, signs of hyperinflation including barrel chest, enlarged lung volume, and poor diaphragmatic excursion prolonged expiratory phase, use of accessory muscles of respiration, sitting in characteristic "tripod" position to facilitate sternocleidomastoid, scalene and intercostal muscles, expiratory wheezing, and odor of smoke or nicotine staining of fingernails. COPD was confirmed by performing spirometry and bronchodilator reversibility testing on patients suspected clinically to be suffering from disease.[7]

Through relevant history and neurological examination – patients with conditions adversely affecting nerve conduction (severe anemia, chronic renal failure, liver failure, chronic alcoholism, congestive cardiac failure, diabetes mellitus, thyroid disorders, neuromuscular disorders, rheumatoid arthritis, and drug abuse) or patients on antiretroviral/ antitubercular drugs which may lead to PNP were excluded.[8] After applying these inclusion and exclusion criteria, 100 cases of COPD in the age group of 25–65 years were selected. Subjects were briefly explained about the procedure and voluntary informed consent was taken.

Spirometry was done using MEDGRAPHICS body plethysmograph. COPD patients classically show a decrease in both FEV and forced vital capacity (FVC). With worsening of the disease severity, there were an increase in lung volumes, total lung capacity, functional residual capacity, and residual volume.

Airflow limitation seen in COPD patients is defined as a post-bronchodilator FEV in 1 s (FEV1) to FVC (forced vital capacity) ratio <0.70, without reversibility to bronchodilators. The severity of airflow limitation in COPD is classified based on Global Initiative for Obstructive Lung Disease (GOLD) criteria.[9]

The cases of COPD were grouped in accordance with these GOLD criteria:

- Group 1: Mild – FEV1 ≥ 80%
- Group 2: Moderate – 50% ≤ FEV1 < 80%
- Group 3: Severe – 30% ≤ FEV1 < 50%.

Nerve conduction studies were performed on median, ulnar, peroneal, and sural nerves using standard protocol and settings as described by Misra and Kalita[6] using NEURO–MEP–NET EMG/NCV/EP (NEUROSOFT TM) Equipment. The apparatus works on a computer with Windows 98 operating system having MS Office 97 package.

The recording electrode, ground electrode, and stimulating electrode are applied to the skin after application of electrode paste. For motor nerve conduction study, the low-frequency filter was set at 2 Hz and high-frequency filter at 10 kHz. For sensory nerve conduction study, the low-frequency filter was set at 5 Hz and high-frequency filter at 3 kHz. The sweep speed was set at 2 ms/division.

The active and reference electrodes, placed 3 cm apart, make up the recording electrode. The active electrode was placed over motor point of the muscle (midpoint between the origin and insertion of the muscle) or nerve segment to be studied. The reference electrode for motor response was positioned on the muscle tendon and for sensory response was placed on the nerve segment to be studied. A skin surface ground electrode was placed between the recording electrode and stimulating electrode. The stimulating electrode, placed on the skin at appropriate sites, was used for stimulation of the nerve with supramaximal stimulus (20–40 mA) at constant current pulses. The position of electrodes is stated in [Tables 1 and 2].[6]

Motor nerve conduction velocity, latency, and amplitude of median, ulnar, and peroneal nerves were recorded in the three groups. Similarly, sensory conduction velocity, latency, and amplitude in median, ulnar, and sural nerves were recorded. Normality test of the sample was conducted using Kolmogorov–Smirnov test in SPSS following which the data for each nerve parameter in the three groups were analyzed using one-way analysis of variance (ANOVA) in SPSS Version 14 and Microsoft Excel database. To study correlation between FEV1% and each of the three parameters of the nerves, Pearson's moment product correlation analysis (direct correlation test) was applied.

RESULTS

Demographic data of the subjects are stated in [Table 3]. [Tables 4 and 5] summarize the mean and standard deviation of nerve conduction parameters recorded in COPD patients as categorized under Group 1 (FEV1 ≥80%), 2 (50% ≤ FEV1 <80%), and 3 (30% ≤ FEV1 <50%) according to FEV1%.

Nerve conduction parameters (conduction velocity, amplitude, and latency) of these three motors and three sensory nerves were compared among the groups divided on the basis of FEV1% as defined in GOLD standard criteria. This statistical analysis was conducted using one-way ANOVA. Motor conduction velocity and amplitude (compound motor action potential) of median, ulnar, and

Table 1: Position of electrodes in motor nerve conduction test.

Motor nerve tested	Recording electrode	Reference electrode	Ground electrode	Stimulating electrode
Median	Abductor pollicis brevis –midway between the distal wrist crease and the first MCP joint	3 cm distal to recording electrode at the first metacarpophalangeal joint	Dorsum of hand	Distally: 3 cm proximal to distal wrist crease near palmaris longus tendon. Proximally: Elbow near the volar crease of the brachial artery pulse
Ulnar	Abductor digiti minimi –midway between the distal wrist crease and the fifth MCP joint	3 cm distal to recording electrode at the fifth metacarpophalangeal joint	Thenar eminence	Distally: 3 cm proximal to distal ulnar crease on the ulnar aspect Proximally: 4 cm distal to the prominence of olecranon at elbow
Peroneal	On extensor digitorum brevis; dorsum of foot	3 cm distal to recording electrode	Below the lateral malleolus	Distally: Over ankle Proximally: Behind the neck of fibula

Table 2: Position of electrodes in sensory nerve conduction test.

Sensory nerve tested	Recording electrode	Reference electrode	Ground electrode	Stimulating electrode
Median	3 cm proximal to distal wrist crease radial to palmaris longus tendon	3 cm proximal to recording electrode	Hypothenar eminence	Cathode: Proximal interphalangeal joint of second digit Anode: 3 cm distal to the cathode
Ulnar	3 cm proximal to the distal wrist crease overlying the ulnar nerve	3 cm proximal to recording electrode	Hypothenar eminence	Cathode: proximal interphalangeal joint of fifth digit Anode: 3 cm distal to cathode
Sural	Between lateral malleolus and tendoachillis	3 cm distal to recording electrode	Above the lateral malleolus of ankle	Cathode: 10–16 cm proximal to recording electrode, distal to lower border of gastrocnemius at the junction of middle and lower third of leg Anode: 3 cm distal

Table 3: Demographic characteristics of subjects.

Variables	Group 1, mild (FEV1 ≥80%)	Group 2, moderate (50% ≤ FEV1 <80%)	Group 3, severe (30% ≤ FEV1 <50%)
Number	34	33	33
Age (years)	50.32±8.79	52.03±10.51	54.15±9.42
Male:female	30:3	29:4	32:1

Table 4: Motor nerve conduction velocity (m/sec), amplitude (millivolts), and latency (milliseconds) in groups formed according to FEV1%.

Group*	Median CV	Median A	Median L	Ulnar CV	Ulnar A	Ulnar L	Peroneal CV	Peroneal A	Peroneal L
1	54.93±4.99	7.62±2.69	3.91±0.52	56.45±5.03	6.85±1.11	3.44±0.69	45.5±5.41	3.86±1.05	6.79±1.49
2	55.05±5.31	8.12±2.25	4.07±0.53	55.61±5.14	7.20±1.26	3.71±0.61	44.94±4.21	3.77±1.27	6.73±1.29
3	54.02±5.32	6.90±1.98	4.11±0.56	55.10±5.21	6.68±1.57	3.68±0.55	43.31±5.44	3.65±1.34	7.05±1.49
P value	0.681	0.109	0.301	0.533	0.279	0.137	0.545	0.783	0.623

*Group according to FEV1% as in GOLD criteria, CV: Conduction velocity, A: Amplitude, L: Latency, $P < 0.05$ = significant

peroneal nerve were found to decrease in groups but this was not statistically significant. Similarly, sensory conduction velocity and amplitude (sensory nerve action potential, SNAP) also showed a fall in median and ulnar nerves. Both were statistically insignificant. Latency recorded in all motor and sensory nerves showed an insignificant rise in groups. Sural nerve conduction velocity and amplitude decreased significantly ($P = 0.002$, $P = 0.003$) in groups formed according to FEV1%.

Two-way ANOVA and direct correlation test were done between FEV1% and nerve conduction parameters in these nerves to establish a causative role of falling FEV1% on fall

of amplitude, conduction velocity, and rise of latency. A positive and strong correlation was found between sural nerve sensory conduction velocity (P = 0.029, r = 0.444) as represented in [Tables 6 and 7] and [Figure 1]. There is no significant correlation between nerve conduction parameters of other sensory and motor nerves with forced expiratory volume at the end of 1 s.

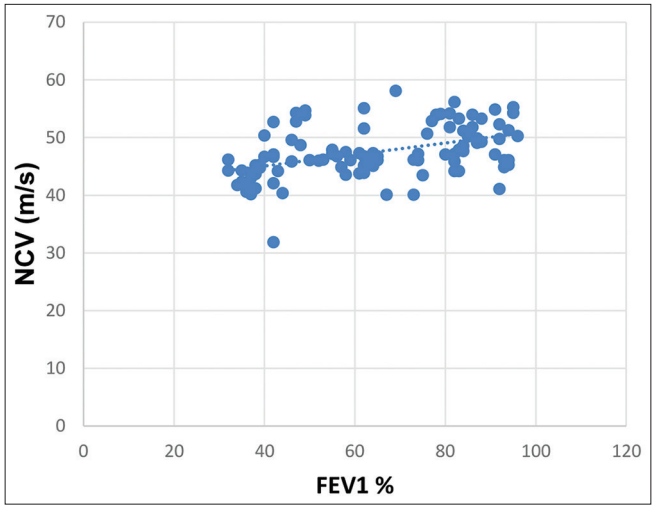

Figure 1: Scatter diagram – correlation between sural sensory conduction velocity (m/s) and FEV1% among chronic obstructive pulmonary disease patients.

DISCUSSION

In the present study, we found significant association between stages of COPD and sural nerve conduction velocity and amplitude which shows that sural neuropathy increases with the severity of the disease. Decrease of both conduction velocity and amplitude indicates the presence of axonal polyneuropathy.[6,10] Our results coincide with Kazi *et al.*[11] who reported subclinical neuropathy in 48 out of 50 COPD patients, involving most frequently the sural sensory nerve. Jann *et al.*[12] have reported axonal polyneuropathy in 19 out of 30 patients and Faden *et al.*[13] in 20 out of 23 COPD patients. These patients were inclusive of those suffering from very severe COPD[9] which was not taken into consideration in this study. Our main focus has been on patients with FEV1% not less than 50% even after bronchodilator therapy.

As shown in [Tables 4 and 5], no significant association between median, peroneal, and ulnar motor conduction parameters and FEV1% was found. This is in contrast with significant ulnar nerve conduction defect noted by Valli *et al.*[14] and according to the involvement of motor neurons. Statistically significant decrease in amplitude and increase in latency in median sensory conduction and a significant slowing down in conduction velocity of median motor nerve conduction with decreasing FEV1% was reported in a study conducted by Agrawal *et al.*[15] Likewise, in a study conducted on 126 COPD cases, significant slowing down in

Table 5: Sensory nerve conduction velocity (m/sec), amplitude (microvolts), and latency (milliseconds) in groups formed according to FEV1%.

Group*	Median CV	Median A	Median L	Ulnar CV	Ulnar A	Ulnar L	Sural CV	Sural A	Sural L
1	54.74±4.96	27.53±7.48	3.11±0.76	51.43±6.35	28.22±9.98	2.69±0.71	49.49±3.94	7.19±3.29	2.52±0.46
2	52.55±6.8	24.84±10.03	3.31±0.80	47.22±8.47	25.99±8.52	2.76±0.81	47.51±4.16	6.48±1.38	2.66±0.53
3	51.7±5.98	22.38±10.35	3.58±0.86	49.45±7.23	23.09±8.34	2.79±0.86	45.72±4.92	5.32±0.99	2.82±0.55
P value	0.102	0.076	0.057	0.081	0.069	0.872	0.002	0.003	0.056

*Group according to FEV1% as in GOLD criteria, CV: Conduction velocity, A: Amplitude, L: Latency, $P < 0.05$ = significant

Table 6: Correlation of FEV1% with motor nerve conduction parameters.

	Median CV	Median A	Median L	Ulnar CV	Ulnar A	Ulnar L	Peroneal CV	Peroneal A	Peroneal L
P value	0.355	0.368	0.526	0.383	0.469	0.549	0.594	0.569	0.539
r-value	0.078	0.148	−0.215	0.065	0.059	−0.202	0.05	−0.140	−0.071

CV: Conduction velocity, A: Amplitude, L: Latency, $P<0.05$=significant

Table 7: Correlation of FEV1% with sensory nerve conduction parameters.

	Median CV	Median A	Median L	Ulnar CV	Ulnar A	Ulnar L	Sural CV	Sural A	Sural L
P value	0.111	0.096	0.558	0.189	0.042	0.514	0.029	0.189	0.538
r-value	0.224	0.173	−0.183	0.137	0.230	−0.048	0.444	0.399	−0.188

CV: Conduction velocity, A: Amplitude, L: Latency, $P<0.05$=significant

median, ulnar, and sural sensory conduction velocities was noted while the mean conduction velocity for the motor nerves was similar to the control group.[16] Peroneal motor conduction velocity abnormality has also been reported.[17]

As shown in [Table 7], we found that the occurrence of PNP is more frequent in the lower extremities and affecting mainly sensory fibers. Narayan and Ferranti[18] have reported this in chronic hypoxemic patients with severe respiratory insufficiency. It is suggested that hypoxia in COPD patients due to chronic airway obstruction is the cause for neuropathic changes. The neuropathic changes in this study have been found to correlate strongly with stage or chronicity of disease.

Neuropathy could also be attributed to inflammatory process spreading from pulmonary circulation into the systemic circulation. Oncel *et al*. and Palange researched on the relation between inflammatory cytokines (TNF-α, IL-6, and IGF-1) and neuropathy in COPD patients but no causative role could be established.[19,20] This could be accounted to a smaller sample size. Therefore, a study with larger number of patients may support the role of oxidative stress in nerve conduction parameter alterations.

CONCLUSION

This study shows that advancement in severity of disease predisposes to neuropathy. Hence, sensory nerve conduction study can be advised routinely and at regular intervals to the patients suffering from increasing severity of COPD for early detection of neuropathy. With this, neuropathic drug can be avoided and supportive therapy added in treatment protocol of these patients. Second, further studies can be undertaken to delineate causative role of inflammatory cytokines in PNP in larger sample size of these patients.

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Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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