Electrophysiological Evaluation Of Peripheral Nerves In Patients With Chronic Obstructive Pulmonary Disease

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Abstract: **Background and objectives:** COPD is the fourth leading cause of death worldwide[1]. Due to COPD hypoxaemia occurs which can cause negative effect on peripheral nervous system. The main aim is to evaluate nerve conduction velocity in patients with COPD to find out neuropathy if present and also to find out correlation among Stages of Chronic Obstructive Pulmonary Disease, severity of hypoxemia, Smoking and peripheral neuropathy. **Method:** For this study 50 cases of COPD having no other apparent pathology that can affect peripheral nerves were included. Their clinical neurological assessment was done and nerve conduction velocity was measured for ulnar, median, sural and peroneal nerves by RMS electromyography. The patients were grouped according to stages of COPD, PaO_2 level and smoking history. **Results:** In this study we found strong positive association of stages of COPD[2] and neuropathy. By electromyography, 96% patients were found to have neuropathy, commonly sensory and most commonly affected nerve was sural nerve. **Interpretation and conclusion:** In this study I found that as severity of disease increases, COPD patients suffer from subclinical neuropathy, so drugs causing neuropathy as adverse reaction should be avoided.

Keywords: chronic obstructive pulmonary disease (COPD), peripheral neuropathy, nerve conduction velocity (NCV)

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Introduction: Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death world-wide[1] and a further increase in the prevalence as well as mortality of the disease is predicted for coming decades. Therefore, there is an impending need to create awareness regarding COPD and help thousands of people who suffer from this disease and die prematurely because of it or its associated complication(s). Chronic hypoxemia developing in COPD patients may lead to peripheral neuropathy[3, 4]. Hypoxic neuropathy is associated with nerve capillary endothelial cell hyperplasia and hypertrophy predisposing to luminal occlusion.When combined with the thickening of nerve perineurium, this may impair the transport of nutrients and oxygen.These mechanisms seem to be applicable to peripheral nerve disfunction and lesion, causing axonal degeneration[5]. Due to hypoxia neuronal gap between nerve cell widens because of that there is impaired transmission of nerve signal between nerve cells because enough oxygen is not available to support nerve cell metabolism. So hypoxia precipitates neuropathy[6]. Peripheral neuropathy in COPD has received scanty attention despite the fact that very often clinicians come across COPD patients having clinical features suggestive of peripheral neuropathy. The presumed etiopathogenic factors are multiple: chronic hypoxia, tobacco smoke, alcoholism, malnutrition and adverse effects of certain drugs.

The aim of this study is to evaluate conduction velocity (CV) and amplitude (A) of peripheral sensory and motor nerves in patients with COPD to find out neuropathy, if present and also to find out correlation of peripheral neuropathy with stages of COPD, severity of hypoxemia and smoking history.

Material and Method:

In this study, I had included fifty patients (46 Male: 4 Female) with COPD attending Chest Disease and Tuberculosis OPD, civil hospital, Ahmedabad. In all the patients COPD was diagnosed by history, symptoms and signs and confirmed by spirometry. Patients having age more than 65 years and those having diabetes mellitus, anemia, chronic renal failure, peripheral circulatory disorder, neoplasm, neurotic drug abuse, alcoholism, severe malnutrition, and liver problems, which may all lead to peripheral neuropathy, were excluded. The study was done with a permission of ethical committee.

All patients were examined for any signs and symptoms of Neuropathy such as tingling, numbness or loss of power.Then all the patients were evaluated by Nerve Conduction Velocity test by RMS electromyography at paraplegia

hospital, followed by blood gas analysis to detect hypoxaemia by automated blood gas analyser in high tech laboratory at Civil Hospital, Ahmedabad, as COPD changes level of blood gases in patients.Nerve Conduction Velocity of following nerves were tested.[7]

Sensory Nerves-Left Ulnar nerve, Left Median nerve, Right and Left Sural nerves, Motor nerves-Left Ulnar nerve, Left Median nerve, Right and Left Peroneal nerves

Subjects were grouped -
According to their percentage of forced expiratory volume in one second FEV_1% values according to Global Initiative for Obstructive Lung Disease[2] (GOLD) criteria for COPD
Group 1: mild - $FEV_1 \geq 80\%$,
Group 2: moderate - $50\% \leq FEV_1 < 80\%$
Group 3: severe - $30\% \leq FEV_1 < 50\%$,
Group 4: very severe $FEV_1 < 30\%$

Accordingto their arterial blood gas values
Group 1: those without respiratory insufficiency - $PaO_2 \geq 60mmHg$
Group 2: those having respiratory insufficiency- $PaO_2 < 60mmHg$

According to their smoking habits Group 1: nonsmokers, Group 2: those with a smoking history of 1-20 bidis/day, Group 3: those with a smoking history over 20 bidis/day.

In this study mean age of all patients was 55.78 ± 8.28 (range 29-64 yrs). 18 patients had never smoked, 12 patients smoked,having ≤ 20 bidis/day and 20 patients having3 > 20 bidis/day. A one sided variation analysis (ANOVA) was used in order to establish the presence of any statistically significant difference of Nerve Conduction Velocity and Amplitude, between the patient groups formed according to FEV_1%, PaO_2 and dose of smoking. FEV_1% values, PaO_2 values, smoking history, Conduction Study and Amplitude of the nerves were analysed by using Pearson's Movent Product Correlation analysis (direct correlation test) to find out any correlation between them.

Results:

Table.1 Sensory Nerve Conduction Velocity (mt/sec) & Amplitude (microvolts) in groups formed according to FEV_1%, PaO_2, Smoking history.

Group according to FEV_1%	Median Sensory-CV	Median Sensory -A	Ulnar Sensory-CV	Ulnar Sensory -A	SuralSensory (Right) –CV	SuralSensory (Right) –A	SuralSensory (Left) -CV	SuralSensory (Left) -A
1	56.786 ± 4.282	28.34 ± 11.86	50.45 ± 4.91	33.03 ± 18.25	49.69 ± 4.3	7.51 ± 3.07	49.25 ± 3.11	7.51 ± 4.23
2	52.65 ± 5.29	22.73 ± 13.67	46.30 ± 10.0	22.3 ± 11.45	45.14 ± 6.43	5.11 ± 1.83	45.12 ± 5.26	5.83 ± 2.69
3	51.19 ± 5.92	20.78 ± 10.58	50.66 ± 5.31	20.09 ± 9.82	38.89 ± 6.36	4.4 ± 0.44	39.34 ± 7.08	5.32 ± 2.35
4	52.94 ± 6.6	32.93 ± 14.05	50.35 ± 5.12	21.59 ± 12.93	30.52 ± 6.86	4.52 ± 0.87	33.16 ± 6.32	3.43 ± 0.69
P	.112	.097	.088	.089	.000	.000	.000	.022
Group according to PaO_2								
1	53.05 ± 5.75	25.49 ± 13.25	49.72 ± 7.22	23.89 ± 13.87	42.03 ± 8.54	5.34 ± 2.13	42.16 ± 7.64	5.61 ± 3.01
2	53.19 ± 6.82	20.13 ± 7.62	51.15 ± 6.37	20.4 ± 4.5	34.39 ± 9.92	4.29 ± 0.5	39.42 ± 11.24	5.13 ± 2.67
P	.964	.431	.704	.621	.096	.330	.509	.761

Group according to smoking history								
1	51.84 ± 6.26	25.27 ± 12.39	49.57 ± 6.23	23.71 + 12.69	42.07 ± 8.82	5.22 ± 2.36	40.33 ± 8.6	5.4 ± 2.76
2	54.44 ± 4.47	24.65 ± 9.5	51.71 ± 4.26	22.71 + 14.1	36.11 ± 9.79	5.08 ± 1.63	41.64 ± 6.85	5.87 ± 3.42
3	53.34 ± 6.04	25.13 ± 15.52	48.95 ± 9.05	24.07 ± 14.19	44.02 ± 7.02	5.39 ± 2.1	43.58 ± 7.81	5.55 ± 2.99
P	.473	.992	.566	.963	.041	.921	.450	.918

Right & Left side sural Nerve Conduction Study and Amplitude shows significant difference in group formed according to FEV_1%.In group formed according to smoking history stastically significant difference found in right sural Nerve Conduction Velocity.

Table.2 Motor Nerve Conduction Velocity (mt/sec) and Amplitude (milli volts) in group formed according to FEV_1%, PaO_2 and smoking history.

Group according to FEV_1%	Median Motor-CV	Median Motor-A	Ulnar Motor-CV	Ulnar Motor-A	Peroneal Motor (Right) –CV	Peroneal Motor (Right)-A	Peroneal Motor (Left)-CV	Peroneal Motor (Left)-A
1	57.4 ± 5.47	8.46 ± 3.96	55.67 ± 5.97	6.61 ± 1.68	44.55 ± 4.72	3.97 ± 1.54	47.69 ± 5.38	4.15 ± 1.07
2	57.1 ± 5.23	9.44 ± 4.53	53.22 ± 10.46	6.92 ± 2.69	45.6 ± 5.44	3.89 + 1.32	42.1 ± 6.1	3.62 ± 2.96
3	59.6 ± 7.28	6.79 ± 2.89	56.04 ± 9.73	7.21 ± 1.83	43.78 ± 5.76	3.74 ± 1.19	42.76 ± 6.17	3.61 ± 1.91
4	57.65 ± 3.18	10.24 ± 7.03	51.72 ± 7.08	5.6 ± 1.5	46.72 ± 4.50	3.9 ± 1.63	44.22 ± 4.79	2.92 ± 1.14
P	.632	.252	.616	.310	.560	.978	.110	.648
Group according to PaO_2								
1	57.95 ± 5.88	8.71 ± 4.61	53.98 ± 8.94	6.69 ± 2.03	44.96 ± 5.11	3.81 ± 1.37	43.95 ± 6.19	3.63 ± 2.12
2	59.31 ± 2.53	6.6 ± 4.59	58.49 ± 6.93	7.02 ± 2.98	45.56 ± 7.14	4.5 ± 0.71	42.24 ± 2.18	3.25 ± 1.05
P	.652	.384	.332	.759	.827	.326	.588	.728
Group according to smoking history								
1	59.41 ± 7.29	9.44 ± 5.59	54.76 ± 10.09	6.89 ± 1.72	43.95 ± 5.1	3.89 ± 1.28	42.56 ± 4.74	3.42 ± 2.35
2	57.34 ± 4.6	8.25 ± 4.81	55.33 ± 7.24	6.73 ± 1.64	46.47 ± 4.90	3.91 ± 1.61	41.9 ± 5.18	2.95 ± 1.19
3	57.28 ± 4.58	7.91 ± 3.45	53.37 ± 8.81	6.53 ± 2.64	45.07± 5.52	3.8 ± 1.29	46.09 ± 6.87	4.14 ± 2.10
P	.461	.583	.812	.875	.438	.967	.083	.257

There is no stastically significant difference of Motor Nerve Conduction Velocity & Amplitude in any groups.

Table.3 correlation of FEV_1% with Amplitude and Conduction Velocity of sensory nerves.

	Median Sensory CV	Median Sensory -A	Ulnar Sensory-CV	Ulnar Sensory -A	Sural Sensory (Right) –CV	Sural Sensory (Right) –A	Sural Sensory (Left) -CV	Sural Sensory (Left) -A	Median Motor-CV	Median Motor-A	Ulnar Motor -CV	Ulnar Motor-A	Peroneal Motor (Right) – CV	Peroneal Motor (Right)-A	Peroneal Motor (Left)-CV	Peroneal Motor (Left)-A
FEV_1 % (r)	.262	-.031	.054	.278	.716	.493	.408	.657	-.069	-.036	.035	.069	-.082	.030	.217	.237
(p)	.066	.831	.709	.051	.000	.000	.003	.000	.632	.804	.812	.635	.570	.838	.130	.097

There is a strong and positive correlation of Conduction Velocity and Amplitude of sural Nerve (Right & Left) & ulnar Sensory Nerve Amplitude with FEV_1%.

Table.4 correlation of PaO2 with Sensory & Motor Nerve Conduction Velocity & Amplitude.

	Median Sensory CV	Median Sensory -A	Ulnar Sensory-CV	Ulnar Sensory -A	Sural Sensory (Right) –CV	Sural Sensory (Right) –A	Sural Sensory (Left) -CV	Sural Sensory (Left) -A	Median Motor-CV	Median Motor-A	Ulnar Motor-CV	Ulnar Motor-A	Peroneal Motor (Right) –CV	Peroneal Motor (Right)-A	Peroneal Motor (Left)-CV	Peroneal Motor (Left)-A
PaO_2 (r)	.006	.232	-.071	.294	.510	.074	.364	.111	-.004	.211	-.069	.030	-.087	-.084	.139	.358
(p)	.964	.106	.624	.038	.000	.611	.009	.442	.980	.142	.636	.835	.548	.561	.334	.011

There is strong and positive correlation of conduction velocity of sural nerve (right and left), amplitude of ulnar sensory nerve and left peroneal motor nerve with PaO_2.So with decrease in PaO_2 there is decrease of amplitude of left side peroneal nerve, which suggests axonal neuropahy, charecterised by decrease in conduction velocity is mild to moderate and amplitude of potentials are usually decreased, means hypoxaemia precipitate axonal motor neuropathy in peroneal nerve.

Discussion: In this study according to Nerve Conduction Velocity test, out of 50 patients, 48 were found to have neuropathy. Therefore 96% of the patients were having neuropathy mainly subclinical, as most of the patients did not have any signs and symptoms of neuropathy.Neuropathy involved sensory nerves, mainly sural nerve and most common changes of neuropathy were of axonal type.

In this study there is significant association and correlation between stages of COPD (according to FEV_1%) with sural nerve conduction velocity and amplitude.So that means as chronicity of disease increases there are chances of sural nerve neuropathy. There is a strong and positive correlation of ulnar sensory nerve amplitude with FEV_1%. That means as FEV_1% decreases there is decrease in ulnar sensory nerve amplitude.There is strong and positive correlation of conduction velocity of sural nerve (right and left), ulnar sensory nerve amplitude and left side peroneal motor nerve amplitude with PaO_2 . That means as PaO_2 decreases there is decrease in sural nerve (Right & Left) conduction velocity, ulnar sensory nerve amplitude and peroneal motor nerve amplitude.There is significant effect of hypoxaemia on conduction velocity of sural nerves, amplitude of ulnar and peroneal nerve.

Our findings coincides with study done by- Jann et al[8] ,who reported the presence of polyneuropathy in 19 out of 30 COPD patients, mostly axonal type.Faden et al[9] reported that 20 out of 23 COPD patients showed subclinical neuropathy,most frequently of sensory nerve,mainly sural nerve. Paramelle et al[10], showed peripheral neuropathy was frequent, predominantly in the lower limbs and the duration of hypoxia correlated with polyneuropathy. Kayacan et al[11] grouped patients of COPD according to level of PaO_2 and detected peripheral neuropathy in 93.8% of the study subjects. Vila and Remond et al[12] also concluded that hypoxemia was related to neuropathy.

Conclusion: In this study there is a strong positive association of stages of Chronic Obstructive Pulmonary Disease according to FEV1% and sural sensory nerve amplitude and conduction velocity. As severity in terms of obstructive changes increases there are more chances of development of sensory neuropathy. As hypoxaemia advances there are increased chances of sural sensory and ulnar sensory neuropathy. Also With advancement of hypoxaemia there are more chances of left peroneal motor amplitude decrease.It means that as hypoxaemia advances that causes axonal neuropathy in motor peroneal nerve. There is stastically significant difference noted in right side sural Nerve Conduction Velocity in groups formed according to smoking history so smoking is one of the factors which affect Nerve Conduction Velocity.

In this study there is involvement of peripheral nerves in 96% patients of chronic obstructive pulmonary disease. Most commonly involved nerves are sural sensory and most frequent type of neuropathy is of Axonal type.

In this study, 96% of patients having neuropathy and Nerve Conduction Velocity being simple, harmless, noninvasive and objective technique along with easy interpretation of result can be used routinely to obtain considerable information and evaluate status of nerves in patients with COPD. This study shows that as hypoxaemia advances (bad COPD control) it predispose to neuropathy, so by good disease control with good medication and awareness of patients we can prevent complications.

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