Original Research Paper

Volume : 5 | Issue : 9 | September 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

Causative Role of Cigarette Smoking in Peripheral Neuropathy in Stable Chronic Obstructive Lung Disease Patients: A Cross-Sectional Study

Medical Science

KEYWORDS : Nerve conduction velocity, Chronic Obstructive Pulmonary Disease, Cigarette Smoking

Dr. Vineeta Chadha — Assistant Professor, Department of Physiology, Government Medical College, Chandrapur

Dr. Surendra S. Shivalkar — Associate Professor, Department of Physiology, Grant Government Medical College, Mumbai

ABSTRACT

Context: *Smoking has been attributed as a causative factor for many health problems. The present study is an attempt to find the influence of smoking on nerve conduction in COPD patients.*

Aims: The study aims to find the causative influence of duration and severity of smoking on nerve conduction parameters in COPD patients.

Settings and Design: *The study was conducted in a Department of Physiology in collaboration with Department of Pulmonary Medicine in a tertiary hospital in Mumbai with prior permission of ethical committee. 100 known cases of COPD in the age group of 25 to 65 years were taken after considering for the relevant exclusion criteria.*

Methods and Material: *In the present study conduction latency, amplitude and velocity were recorded as per the standard protocol in median, ulnar, peroneal motor and sural sensory nerves.*

Statistical analysis used: Pearson correlation between motor and sensory nerve conduction velocity, amplitude and latency with smoking history was studied.

Results: *On analysis, strong and negative correlation was found between conduction velocity of sural nerve and smoking history in pack years (r=0.411).*

Conclusions: *Airflow limitation is a causative factor for sensory neuropathy in COPD patients.*

Introduction:

Chronic Obstructive Pulmonary Disease (COPD) is attributed to airway obstruction and systemic features of the disease[1] caused due to multiple factors such as systemic inflammation, oxidative stress, hypoxemia and smoking.[2]

Lindberg et al. in a Swedish cohort study observed population-attributable fraction to smoking as a cause of COPD as 76.2 per cent.[3] Jindal et al suggested that bidi and cigarette smoking is an important factor causing COPD in India.[4]

The purpose of this study is to establish a possible relationship between peripheral neuropathy (PNP) and duration of smoking in COPD patients.

Subjects and Methods:

The study was conducted in a Department of Physiology in collaboration with Department of Pulmonary Medicine in a tertiary hospital in Mumbai with prior permission of ethical committee. 100 known cases of COPD in the age group of 25 to 65 years were selected. Through relevant history & neurological examination patients with conditions (severe anaemia, chronic renal failure, liver failure, chronic alcoholism, congestive cardiac failure, diabetes mellitus, thyroid disorders, neuromuscular disorders, leprosy, rheumatoid arthritis, drug abuse) or antitubercular / antiretroviral drugs which may lead to peripheral neuropathy were excluded.[5] A brief explanation of the procedure was given to the subjects and voluntary informed consent was taken.

Spirometry and bronchodilator reversibility testing was done to diagnose COPD. Spirometry was done using MED – GRAPHICS Body Plethysmograph. Smoking history was obtained. Subjects were questioned about the duration of smoking and number of cigarettes or bidi smoked per day. Pack years of smoking was calculated from this history.

Nerve conduction studies were performed on Median, Ulnar, Peroneal and Sural nerves using standard protocol and settings as described by U. K. Misra and J.Kalita[6] using NEURO – MEP – NET EMG/NCV/EP (NEUROSOFT TM) Equipment.

Results:

Data was statistically analysed after adjusting for age and sex. Mean pack years of smoking at presentation was 30.07 ± 8.81.

Pearson correlation between motor and sensory nerve conduction velocity, amplitude and latency with smoking history was studied as shown in table 1 and 2.

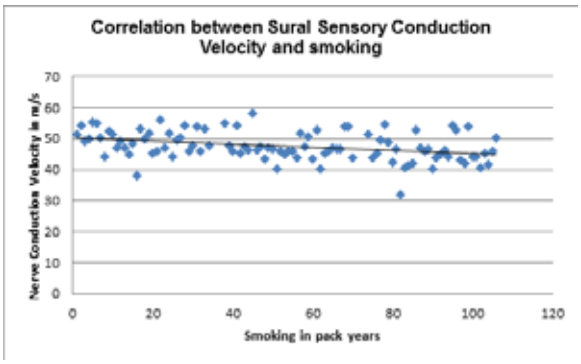
Table 1: Pearson Correlation of Median, Ulnar, Peroneal motor nerve conduction velocity (CV in m/sec), Amplitude (mV) and latency (millisecond) with smoking

Motor Nerve	r value		
	CV	Amplitude	Latency
Median	-0.072	-0.054	0.162
Ulnar	-0.044	-0.018	0.138
Peroneal	-0.097	-0.143	0.190

Table 2: Pearson Correlation of Median, Ulnar, Peroneal and Sural Nerve motor and sensory conduction velocity (m/sec), Amplitude (μV) and latency (millisecond) with smoking

Sensory Nerve	r value		
	CV	Amplitude	Latency
Median	-0.283	-0.134	0.133
Ulnar	-0.114	-0.049	0.145
Sural	-0.411	-0.194	0.043

Figure 1: Scatter diagram - Correlation between Sural Sensory Nerve Conduction Velocity in m/s and smoking among COPD patients



There is no correlation between ulnar nerve motor and sensory or peroneal nerve motor conduction velocity, amplitude and latency with smoking. There is negative correlation between sural nerve sensory conduction velocity and smoking as sown in Figure 1. There is no correlation between sural sensory amplitude and latency with smoking.

Discussion:

Previous studies have shown that the risk of COPD rises as total exposure to smoke increases.[7] A study conducted by Laniado - Laborín R. claims that 20% of smokers will get COPD and among lifelong smokers almost half will suffer from COPD.[8] Volume of air exhaled within 1 second of forced expiratory manoeuvre (FEV1) declines with the intensity of cigarette smoking expressed in pack-years (average number of packs of cigarette smoked per day multiplied by total number of years of smoking). This accounts for higher prevalence of COPD with increase in age. Hypoxemia and cigarette smoking increase the severity of COPD, causing a rise in axonal neuropathy especially affecting sensory fibres.[9,10]

The results of the study are in accordance with Poza JJ et al[11] who conducted a prospective study in 30 COPD patients with no known causes of PNP. In their study PNP was found in 27% of patients on clinical examination which increased to 87% on neurophysiological study. This and a study conducted by Gupta et al[12] report a longer latent period and decrement in conduction velocity suggesting predominantly sensory abnormality with axonal polyneuropathy.

Similar to this study, Gokhan Asal et al[13] and Karishmabanu Kazi et al[14] observed negative correlation between sural sensory nerve conduction velocity and duration of smoking on cliniconeurological assessment and electromyography.

Our findings were in accordance with Faden at al who included all smokers in their study and suggested that exposure to nicotine like substances in cigarette smoke for longer duration may cause toxic effects on the peripheral nerves.[15]

Agrawal et al. studied 30 smoker COPD patients and found that 17% of patients had PNP related to smoking habits and duration of illness. In their study 5 COPD patients smoked severely (≥ 45 pack years of cigarette) as compared to the other patients (35.64 ± 10.96 pack years). In contrast to the present study these patients with PNP had severe airflow obstruction and decreased amplitude and conduction velocity of median sensory and ulnar sensory nerve along with sural sensory nerve. The electrophysiological analysis revealed that they had a predominant sensory, axonal polyneuropathy with mild motor nerve involvement.[8]

In contrast, Agusti et al found no difference in neurophysiological studies between patients with or without smoking exposure. They found PNP to be related with the severity of disease measured by FEV1. Spreading or spilling over of an inflammatory process into the systemic circulation might be a contributing factor for development of PNP.[16]

Cigarette smoking affects neural function by causing vasoconstriction and damaging blood vessels due to atherosclerosis and plaque formation. As a result blood supply and oxygen delivery to the nerve fibers decreases (neural ischemia). Smoking also brings about a rise in blood cholesterol level which predisposes to the atherosclerosis.[17] Smokers with severity of smoking ≥60 pack years have higher frequency of neuropathy. High level of carboxyhaemoglobin in smokers leads to slowing in nerve conduction.[18]

Smoking may disrupt nerve Na^+ - K^+ ATPase activity due to oxidative stress causing derangement in function of unmyelinated nerve fibre as in diabetic neuropathy.[19] Dysfunction of sural nerve conduction could be due to subclinical changes in myelin sheath.[20]

Studies have shown an elevation in serum levels of C-reactive protein (CRP), tumour necrosis factor α (TNF-α), interleukin 6 (IL-6) and other markers of systemic inflammation in stable patients with COPD. Systemic effects in COPD patients have been reported to be due to systemic inflammation. Therefore, PNP could be result of systemic inflammation in patients with or without smoking.[21]

Some researchers have shown no relation between PNP and proinflammatory cytokines such as TNF-α, IL-6, insulin-like growth factor 1 (IGF-1) and CRP.[22] This may be due to lesser number of patients in these studies. Therefore, a study with large sample size may be undertaken to substantiate the role of oxidative stress in nerve conduction alterations among cigarette smokers helping to delineate a causative role of systemic inflammation due to COPD and neurophysiological effects of the disease.[23]

Hence, smoking is strongly and negatively correlated with sural nerve conduction velocity and amplitude in patients of COPD suggesting predominant axonal, sensory neuropathy. Further studies can be undertaken to establish a causative role of inflammatory biomarkers for development of PNP in COPD patients.

References:

1. ICMR-MRC Workshop. Building Indo−UK Collaboration in chronic diseases; 2009. p.16
2. Barnes PJ, Celli BR. Systemic manifestations and comorbidities of COPD. Eur Respir J 2009; 33: 1165-85.
3. Lindberg A, Eriksson B, Larsson LG, Rönmark E, Sandström T, Lundbäck B, et al. Seven-year cumulative incidence of COPD in an age-stratified general population sample. Chest 2006; 129 : 879-85
4. Jindal SK, Aggarwal AN, Chaudhry K, Chhabra SK, D'Souza GA, Gupta D, et al. Asthma Epidemiology Study Group. A multicentric study on epidemiology of chronic obstructive pulmonary disease and its relationship with tobacco smoking and environmental tobacco smoke exposure. Indian J Chest Dis Allied Sci 2006; 48: 23-9.
5. Kimura J. Principles and pitfalls of nerve conduction studies. Ann Neurol 1984; 16: 415-429.
6. Misra U K, Kalita J. Clinical Neurophysiology, 2nd Edition: 1-128.

Volume : 5 | Issue : 9 | September 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

7. Goldman, Lee. Goldman's Cecil medicine (24th ed.). Philadelphia: Elsevier/Saunders. 2012. p. 537
8. Laniado-Laborin, R. "Smoking and chronic obstructive pulmonary disease (COPD). Parallel epidemics of the 21st century". International journal of environmental research and public health. 2009. 6 (1): 209–24.
9. Kayacan O, Beder S, Deda G, Karnak D. Neurophysiological changes in COPD patients with chronic respiratory insufficiency. Acta Neurol Belg 2001; 101:160-5
10. Agrawal D, Vohra R, Gupta P P, Sood S; Subclinical peripheral neuropathy in stable middle-aged patients with chronic obstructive pulmonary disease; Singapore Med J 2007; 48 (10) : 887
11. Poza JJ, Marti-Masso JF: Peripheral neuropathy associated with chronic obstructive pulmonary disease. Neurologia, 1997 12(9): 189-94
12. Gupta PP, Agarwal D. Chronic obstructive pulmonary disease and peripheral neuropathy. Lung India 2006; 23:25-33
13. Gokhan Asal, Aydan Cakan, Ahmet Emin Erbaycu, Fievket Dereli, Ayfle Ozsoz, Hakan Edipolu, Behiye Ozer. Electromyographic Evaluation of Peripheral Nerves in Chronic Obstructive Pulmonary Disease; Turkish Respiratory Journal, August 2003, Vol.4, No.2
14. Karishmabanu Kazi, Anju Mehta, Mansur Mulla. Electrophysiological Evaluation Of Peripheral Nerves In Patients With Chronic Obstructive Pulmonary Disease. IJBAP, Vol 1(1) 2012: 83-87
15. Faden A, Mendoza E, Flynn F. Subclinical neuropathy associated with chronic obstructive pulmonary disease: possible pathophysiologic role of smoking. Arch Neurol 1981; 38: 639-42.
16. Agusti AG, Noguera A, Sauleda J, Sala E, Pons J, Busquets X. Systemic effects of chronic obstructive pulmonary disease. Eur Respir J 2003; 21: 347-60.
17. Brambilla C, Paramelle B, Vila A, et al. Peripheral neuropathies and chronic obstructive pulmonary disease. Electrophysiological and histopathological study. Am Rev Respir Dis 1986; 133: A-62.
18. Narayan M, Ferranti R. Nerve conduction impairment in patients with respiratory insufficiency and severe chronic hypoxemia. Arch Phys Med Rehabil 1978; 59:188-92
19. Kowluru R. A., Kern T. S., Engerman R. L., Armstrong D. Abnormalities of retinal metabolism in diabetes or experimental galactosemia. III. Effects of antioxidants. Diabetes, 1996, 45: 1233-1237
20. Husstedt IW, Grotemeyer KH, Schlake HP, Brune GG; Dysfunction of the sural nerve in cigarette smokers; EG EMG Z Elektroenzephalogr Elektromyogr Verwandte Geb. 1988 Sep;19(3):161-4
21. Kaddah S, Rashed L, Obaia E, Sabry D. A preliminary study: matrix metalloproteinase expression as an indicator of the hazards of shisha (nargila) smoking. Arch Med Sci 2009; 5: 570-6.
22. Cagatay Oncel, Sevin Baser, Mustafa Cam, Beyza Akdag, Betul Taspinar, Fatma Evyapan; Peripheral neuropathy in chronic obstructive pulmonary disease; COPD Journal of Chronic Obstructive Pulmonary Disease 02/2010; 7(1):11-6.
23. Palange P, Testa U, Huertas A, et al. Circulating haemopoietic and endothelial progenitor cells are decreased in COPD. Eur Respir J 2006; 27: 529-41.