Original Article

Cigarette Smoke Induced Sural Nerve Dysfunction in Young Male Subjects

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Abstract

Background: *Cigarette smoking has been attributed as a causative factor for many cardiovascular and respiratory diseases. Increasing evidence suggests that chronic smoking also alters neuronal function and can lead to neuronal injury in the peripheral nervous system. Sural nerve conduction study is an important electrodiagnostic test for early detection of peripheral nerve dysfunction.*

Objectives: *To observe the effects of cigarette smoking on the electrophysiological status of the sural nerve in apparently healthy young male smokers.*

Materials and Methods: *This case-control study was conducted in the Department of Physiology, Sir Salimullah Medical College, Dhaka, from July 2017 to June 2018. Thirty apparently healthy male cigarette smokers aged 25 to 40 years were included in the study group. Another thirty age, sex, and BMI matched non-smoker healthy subjects were controls. Nerve conduction parameters (latency, amplitude, and sensory nerve conduction velocity) of the sural nerve were studied by standard methods, using standard nerve conduction study and electromyography machine in the Department of Neurology, Dhaka Medical College Hospital. For statistical analysis, unpaired t test was done.*

Results: *In this study, the latency of sural nerve was significantly prolonged ($p < 0.001$), whereas amplitude and sensory nerve conduction velocity were significantly reduced ($p < 0.001$) in cigarette smokers in comparison to non-smokers. Among the cigarette smokers, 20% showed evidence of subclinical impairment in sural nerve function.*

Conclusion: *Chronic cigarette smoking causes dysfunction of sural nerve in young male subjects.*

Key words: *Cigarette Smoking, Sensory Nerve Conduction Study, Sural Nerve Dysfunction, Peripheral Neuropathy.*

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Introduction

Tobacco is one of the major public health threats that kills more than 8 million people each year, and the burden of tobacco-related illness is heaviest in developing countries.[1] Currently, there are approximately 1.5 million adults suffering from tobacco-attributable diseases in Bangladesh.[2]

The most prevalent way that people use tobacco is by smoking cigarettes.[1] It causes chronic obstructive pulmonary disease, coronary heart disease, peripheral vascular disease, and cancers of the mouth, lung, and oesophagus.[3] According to recent studies, the toxins in cigarette smoke also have deleterious effects on peripheral nerves, which can result in peripheral neuropathy.[4-6]

The nerve conduction study can confirm the presence and extent of peripheral nerve damage, including alterations of function that are not detected clinically.[7] Significant slowing of the nerve conduction velocity suggests impaired saltatory conduction due to demyelination, and a smaller amplitude reflects a reduction in the overall number of functioning axons.[8]

Most of the nerve dysfunctions initiate in the sensory nerves of the lower extremities.[9] The sural nerve is the most tested sensory nerve in the lower extremities for the diagnosis of peripheral neuropathies.[10] It is a cutaneous nerve of the posterolateral calf that provide innervation to the skin of the distal one-third of the lower leg.[11] Hence, sural neuropathy usually results in sensory changes in the posterolateral aspect of the leg as well as the dorsolateral foot which may occasionally be accompanied by paresthesia and dysesthesia.[12]

A literature review suggests that smoking causes peripheral neuropathy in smokers with chronic obstructive pulmonary

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disease, though the prevalence varied markedly from one study to another. However, it is still unknown whether smoking affects neural function in subjects without pre-existing pulmonary disease. Therefore, we investigated the impact of smoking on sural nerve conduction parameters in apparently healthy young male cigarette smokers.

Materials and Methods

The present case-control study was carried out in the Department of Physiology, Sir Salimullah Medical College, Dhaka, from July 2017 to June 2018, on 30 apparently healthy male daily cigarette smokers, aged 25 to 40 years, who take at least 10 sticks per day and have a smoking history of more than 10 pack years. For comparison, 30 apparently healthy male subjects with similar age, BMI and socioeconomic status who never had any addiction related to tobacco were selected as controls. The subjects were enrolled from the hospital staff members of Sir Salimullah Medical College and Mitford Hospital and also from Dhaka Medical College Hospital by consecutive purposive sampling. The protocol for this study was approved by the Institutional Ethics Committee (IEC) of Sir Salimullah Medical College. Subjects with a history of any major illness like hypertension, diabetes mellitus, peripheral neuropathy, or other neurological disorders, cardiac, renal, or thyroid diseases, or a history of addiction to other tobacco products or alcohol were not included in the study.

After a briefing about the study, written informed consent were taken from the participants. A detailed personal and medical history was taken, and a thorough physical examination was done. Cigarette smokers were interviewed about smoking duration and the average number of cigarettes smoked per day. Then the pack year of smoking was calculated by multiplying the number of packs of cigarettes smoked per day by the number of years the person has smoked. The sural nerve conduction study was performed using a fully computerised NCS and EMG machine (Nihon Kohden Neuropack, Japan) by standard method in the Department of Neurology, Dhaka Medical College Hospital.

The subjects had stopped smoking for an hour before the test in the morning. The procedure was explained to each subject to ensure maximum comfort and compliance. They were requested to lie comfortably on the bed in a supine position. The temperature was maintained at 25-28 ^{o}C in an air-conditioned room. To obtain the highest possible electrical conductivity, the recording and stimulating sites were thoroughly cleansed with spirit. The active recording electrode was placed at the back of the lateral malleolus, and the reference electrode was placed 3-4 cm distally. The ground electrode was positioned between the stimulating and recording sites. An antidromic measurement was done by stimulating the left sural nerve at the posterior-lateral calf. A SNAP was recorded and analysed for the onset latency, amplitude, and SNCV.

The data were expressed as mean ± SD (standard deviation). The statistical analysis was done using the statistical package of social science (SPSS) for Windows version 22. Unpaired t test was done to compare data between two groups. A p value of $\leq$ 0.05 was accepted as the level of significance.

Results

The baseline general characteristics of the subjects in both groups are presented in table I. The sensory nerve conduction parameters (latency, amplitude, and sensory nerve conduction velocity) of the sural nerve are presented in table II. In this study, the mean latency of the sural nerve was significantly prolonged ($p < 0.001$), whereas amplitude and sensory nerve conduction velocity were significantly reduced ($p < 0.001$) in cigarette smokers in comparison to controls. Again, the distribution of sural nerve conduction study showed that 20% of cigarette smokers had subclinical impairment of sural nerve function (Figure 1).

Table I: General characteristics of the subjects in both groups (N=60)

Parameters	Non-smokers (n=30)	Cigarette Smokers (n=30)	p value
Age (years)	33.27 ± 4.70 (25 - 40)	32.77 ± 4.30 (25 - 40)	0.669
Weight (kg)	68.86 ± 4.12 (60 - 75)	67.22 ± 3.94 (58 - 74)	0.118
BMI (kg/m^2)	23.48 ± 1.32 (19.82 - 25.35)	22.97 ± 1.17 (20.55 - 24.91)	0.115
Systolic BP (mm of Hg)	120.17 ± 7.71 (100 - 130)	122.83 ± 5.52 (110 - 130)	0.129
Diastolic BP (mm of Hg)	70.67 ± 6.91 (60 - 80)	73.00 ± 6.77 (60 - 85)	0.192
FBG (mmol/L)	4.80 ± 0.81 (3.42 - 5.96)	4.91 ± 0.73 (3.54 - 5.98)	0.585
S. Creatinine (mg/dl)	0.93 ± 0.17 (0.7 - 1.3)	0.99 ± 0.19 (0.7 - 1.4)	0.203

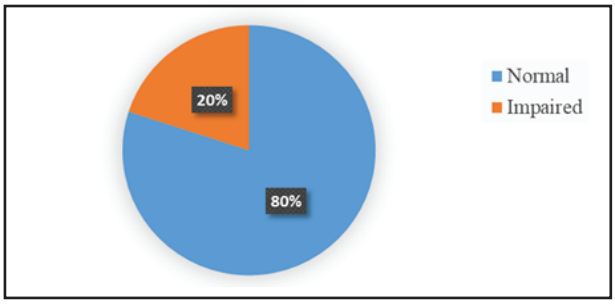
Data were expressed as mean ± SD. Figure in parentheses indicate ranges; N = total number of subjects; n = number of subjects in each group.

Table II: Sural nerve conduction parameters in cigarette smokers and non-smokers (N=60)

Parameters	Non-smokers (n=30)	Cigarette smokers (n=30)	p value
Latency (ms)	1.76 ± 0.18 (1.37- 1.99)	2.14 ± 0.30 (1.5 - 2.67)	<0.001***
Amplitude (μV)	29.43 ± 9.23 (12.10 - 42.04)	20.64 ± 8.21 (11.10 - 40.70)	<0.001***
SNCV (m/s)	54.71 ± 5.25 (45.2 - 64.7)	43.69 ± 4.65 (38.0 - 55.3)	<0.001***

Data were expressed as mean ± SD. Figure in parentheses indicate ranges; Statistical analysis was done by unpaired t test; N = total number of subjects; n = number of subjects in each group; SNCV = sensory nerve conduction velocity; *** = p < 0.001.

Figure 1: Distribution of cigarette smokers according to sural nerve function status.



Discussion

The present study was conducted to evaluate the influence of cigarette smoking on the electrophysiological parameters (latency, amplitude, and sensory nerve conduction velocity) of the sural nerve. In this study, highly significant prolongation of mean latency and highly significant reduction of sensory nerve conduction velocity were observed in apparently healthy male cigarette smokers compared to controls. These findings were almost similar to the results of previous studies, although the inclusion criteria for the study subjects and method were different. Arora et al. conducted a study where the smokers were further categorized into three groups: light, moderate, and heavy, based on their smoking index.[13] They found highly significant prolongation of distal latency and significant reduction of sensory nerve conduction velocity when each smoker group was compared with non-smokers. In another study, Chavan et al. reported a significant reduction in sural nerve conduction velocity in both the moderate and heavy smoker groups in comparison to non-smokers, but there was no statistically significant difference between the mild smoker and non-smoker groups.[14] However, our study quantified smoking exposure in pack years and compared the electrophysiological findings across two groups: non-smokers and chronic cigarette smokers. Again, in this study, a highly significant reduction in amplitude was found in cigarette smokers compared to non-smokers. This decline might have been attributed to axonal loss, as amplitude reflects the number of functioning axons. Arora et al. also observed a significant reduction in amplitude while comparing light, moderate, and heavy smokers to non-smokers.[13] However, Chavan et al. noted a significantly decreased sural nerve conduction amplitude, specifically among heavy smokers; they did not find a statistical difference between the mild smoker and non-smoker groups, nor between the moderate smoker and non-smoker groups.[15]

We also found that 20% of apparently healthy cigarette smokers had electrophysiological evidence of subclinical impairment of the sural nerve. This finding could not be compared due to the unavailability of published data since most of the previous works were primarily focused on smokers with chronic obstructive pulmonary disease. However, the sural nerve was the most commonly affected nerve among COPD patients with peripheral neuropathies.[5,16]

In the current study, the neurophysiological findings revealed the dysfunction of the sural nerve in apparently healthy cigarette smokers and these data indicate that the onset of neural dysfunction commonly occurs during the early years of smoking. Therefore, effective measures should be taken for smoking cessation at a young age to prevent potentially fatal neurological outcomes. It is well established that nerve conduction depends on the insulating properties of myelin.[17] Demyelination causes blockage of nerve conduction and slowing of nerve conduction velocity.[7] The precise etiology of peripheral nerve demyelination and axonal degeneration in cigarette smokers is still unresolved. Some researchers have suggested that oxidative stress may have a potential role in the development of demyelination.[18] Cigarette smoking can induce oxidative stress by augmenting lipid peroxidation.[19] Myelin sheath is enriched in lipids and highly vulnerable to oxidative stress.[20] According to some authors, the axonal degeneration associated with myelin loss in demyelinating diseases is related to oxidative stress caused by impaired oxidative phosphorylation.[21] Furthermore, Yu et al. showed that cigarette smoking inhibits the expression of genes needed for myelin synthesis and maintenance.[22]

Conclusion

From the results of this study, it could be concluded that chronic cigarette smoking induces neuropathic changes in the sural nerve. Therefore, electrophysiological evaluation of the sural nerve function could be done for early prediction of peripheral neuropathy in young smokers to prevent further neurological damage.

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