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CORRELATION OF SMOKING INDEX WITH THE MOTOR NERVE CONDUCTION STUDY IN MILD, MODERATE AND HEAVY SMOKERS

Physiology

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ABSTRACT

Tobacco use, and in particular smoking, is the largest cause of preventable death among adults in India, as it is globally. Already 1 in 5 of all adult male deaths and 1 in 20 of all adult female deaths at ages 30-69 are due to smoking. Higher carboxyhemoglobin levels in the circulating blood found in smokers leads to slowing of nerve conduction by its direct action over the myelin sheath. Nicotine too has a direct effect on the myelin sheath. Previous studies have found sensory neuropathy in smokers. Smokers. But motor neuropathy is not diagnosed until the appearance of symptoms and is not yet an established fact. We performed Nerve Conduction Study (NCS) on motor nerves of both upper and lower limbs among mild, moderate and heavy smokers as well as in non-smokers. Motor nerve conduction velocity (MNCV) and Compound Muscle action potential (amplitude) of peripheral motor nerves in both upper & lower limbs are significantly reduced in smokers as compared to non-smokers and distal latency is also highly significantly prolonged in smokers. The results have also revealed dose-response relationship with the smoking. Hence, Nerve conduction studies can diagnose neuropathic changes even before the appearance of frank neuropathyinsmokers.

KEYWORDS

Smokers, Neuropathy, Smoking Index, Motor Nerves, Nerve Conduction Study

INTRODUCTION

The tobacco epidemic is one of the biggest public health threats the world has ever faced.[1] Tobacco use, and in particular smoking, is the largest cause of preventable death among adults in India, as it is globally. Already 1 in 5 of all adult male deaths and 1 in 20 of all adult female deaths at ages 30-69 are due to smoking.[2]

Tobacco smoke is a toxic mix of more than 7,000 chemical[3]. Some of the chemicals in cigarette smoke/bidi like nicotine, tar, carbon monoxide, cyanide etc. are toxic to the peripheral nerves. They cause a direct toxic effect on the myelin sheath. Although demyelination and axonal damage might co-exist in CO intoxication, demyelination more than axonal damage is suggested in the literature.[4]

Nerve conduction studies are considered as the most sensitive indices of the severity of peripheral neuropathy, including alterations in function that are not recognized clinically.[5] NCS are abnormal when pathological changes are present in myelin, nodes of Ranvier, and axons. The NCS findings correlate with the clinical endpoints and nerve potential amplitudes reflect the degree of nerve fibre loss. Thus with the help of NCS diagnosis of neuropathy can be made early. Previous literature on smokers have studied only sensory nerves , the status of peripheral nerves is not mentioned. Hence, in this study, we have studied motor nerves in both upper and lower limbs in mild, moderate and heavy smokers. We have also tried to establish the correlation of smoking index with the extent of damage to peripheral nerves.

MATERIALS & METHODS

This study was carried out in the Neurophysiology lab of Department of Physiology in People's College of Medical Sciences and Research Centre, Bhopal (M.P.). The study was done in 40 smokers of age group 20-40 years who were apparentlyhealthy with duration of smoking of at least 2 bidis/cigarettes per day for the last 5 years. The results were compared with a comparison group of non-smokers of the same age-group.

The individuals who are asymptomatic and (in our situation) have no significant disease or physical condition that prevents them from engaging in physical activity are called as apparently Healthy as per American Council on Exercise[6].

Exclusion of Subjects: Diabetes mellitus, Peripheral circulation disorder, chronic renal failure, thyroid disorder, history of intake of drugs causing peripheral neuropathy , severe malnutrition, anaemia & alcoholism, any bleeding tendency ,history of pace-maker placement, cardio-implant, implanted intracranial device

Grouping of Subjects:

Smoking Index[7] was used to determine smoking exposure of the body quantitatively.

Smoking Index= average number of cigarettes smoked per day in last seven days x duration of smoking in years

According to Smoking Index the smokers were classified into:

Group 1. Light smokers: Smoking index < 100
Group 2. Moderate smokers: Smoking index 101-200
Group 3. Heavy smokers: Smoking index >200
Group 4. Non-Smokers

As per the criteria of Smoking Index, the moderate smokers were more common among the population studied (45%) followed by light smokers (30.0%) and heavy smokers (25.0%) Most of the smokers included in the study smoked both cigarette and bidi.

METHODOLOGY: Subjects were selected after taking meticulous history as per the inclusion and exclusion criteria from the campus of PCMS & RC, Bhopal. The study subjects were instructed to avoid smoking for 3 hours before examination. The cases were evaluated for any signs and symptoms of neuropathy.

Neuroperfect Machine – "EMG, NCV, EP – Medicaid Machine 2000" in the Neurophysiology laboratory of department of Physiology, PCMS & RC, Bhopal was used to perform nerve conduction study in the following nerves

In both upper limbs: Median motor & Ulnar motor nerves
In both lower limbs: Posterior TIbial, Common Peroneal nerves

Principles OF NCV-:

Nerve conduction studies can help distinguish axon loss (loss of amplitude) from demyelinating conditions (slowed conduction).

Nerve Conduction Study requires an external stimulation that initiates depolarization simultaneously in all axons of the nerve to produce a recordable response. The response is recorded by stimulating the nerve at two different points along its course.

Nerve Conduction velocity (mt/sec.) is calculated by measuring the distance between two points of stimulation (mm) which is divided by the latency difference (msec).

Conduction velocity(mt/sec) = Distance (mm) / proximal - distal latency (ms)

Procedure of NCV:
The subjects was made to lie down comfortably in supine position, Instrument was kept out of view of subject , Procedure was explain to the subject before the test then asked the subject to be relaxed. Surface electrodes were utilized for recording and stimulation of nerves and were fixed to subjects skin by adhesive tape.

To assure adequate contact, skin was cleaned with the spirit and electrode gel was used / between the electrodes and the skin for proper conduction.

The distance between the first, second stimuli was measured by a flexible tape measure millimeters and Stimulation by a supramaximal technique.

Table A below showing placement of electrodes for Motor Nerve Conduction study[8].

Upper Limb Nerves	Recording site	Stimulation site	
		Proximal	**Distal**
1. **Median** Motor	Abductor Pollicis Brevis	Elbow(near volar crease of brachial Pulse)	Wrist(3cm proximal to distal crease)
2. **Ulnar** Motor	Abductor Digiti Minimi	Elbow	Wrist
Lower Limb Nerves	**Recording site**	**Stimulation site**	
		Proximal	**Distal**
1.**Common Peroneal** Motor	Extensor digitorum brevis	Fibular head	Ankle
2.Tibial Motor	Abductor hallucis brevis	Popliteal fossa	Ankle

Table B Showing Placement Site for Reference[8]:

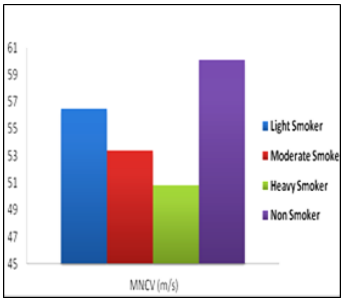
Sr. No.	Nerves	Placement site
1.	Median	Placed near 1st metacarpo-phalangeal joint.
2.	Ulnar	Placed near 5th metacarpo-phalangeal joint.
3.	Peroneal	Placed near 4th metatarso-phalangeal joint.
4.	Tibial	Placed near 1st metatarso-phalangeal joint.
5.	Sural	Placed near 5th metatarso-phalangeal joint

The parameters analyzed for Motor Nerves:
Motor Nerve Conduction Velocity (MNCV) in metre/sec.
Compound Muscle Action Potential(CMAP)- Amplitude in microvolts
Distal Latency of motor nerve DL(M) in millisec.
Average of MNCV, CMAP & DL (M) of all the 4 nerves is taken and results are tabulated in table 1. The data is statistically analyzed by one way ANOVA.

Table 1: Effect of Smoking on Motor Nerve Conduction study of Both upper and Lower limbs (One Way ANOVA)

Parameter	Group1 Light smoker	Group2 Moderate smoker	Group3 Heavy Smoker	Group 4 Non-smoker	ANOVA F value	P Value
MNCV (m/sec)	56.49±1.54	53.39±1.75	50.80±0.52	60±6.6	26.657	<0.05 **(S)**
CMAP(μV)	7.39±2.16	6.21±1.86	5.24±1.3	7.5±3.46	250	<0.05 **(S)**
DL(Motor) (ms)	3.07±.1.18	3.28±1.05	4.8±0.87	2.83±1.14	400	<0.001 **(HS)**
Values expressed as Mean± Standard Deviation P<0.05 or P = 0.05 Significant, P<0.001or P=0.001 Highly Significant						

Observations from table 1:
Motor nerve conduction velocity (MNCV) and Compound Muscle action potential (CMAP means amplitude)of peripheral motor nerves in both upper & lower limbs are significantly reduced in smokers as compared to non-smokers while distal latency of peripheral motor nerves is highly significantly prolonged in smokers.

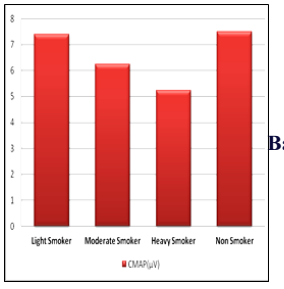


Bar Diagram 1A showing MNCV

Table 2: Tukey's Post Hoc Analysis for Intragroup comparison of MNCV

Groups	MEAN DIFFERENCE	P VALUE
1 vs 2	3.09167	0.335(NS)
1vs3	5.68700	0.041(NS)
1vs4	7.58750	<0.001(HS)
2vs3	2.59533	0.540 (NS)
2vs4	6.67917	<0.001(HS)
3vs4	-9.27450	<0.001(HS)

Observations table 2:
Tukey's post hoc analysis shows difference in the mean values of MNCV among light, moderate & heavy smokers are not significant. When results are compared with the non-smokers, highly significant decrease in MNCV values are seen in all smoker groups.

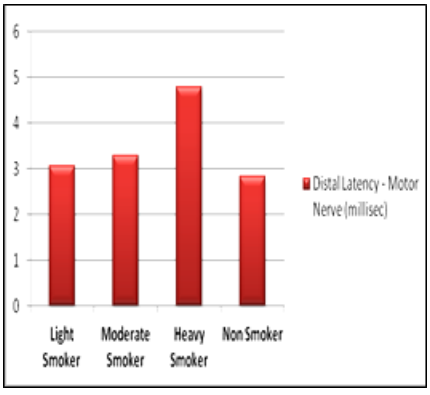


Bar Diagram 1B showing CMAP

Table 3: Tukey's Post Hoc Analysis for Intragroup comparison of CMAP

Groups	MEAN DIFFERENCE	P VALUE
1 vs 2	1.18	<0.001(HS)
1vs3	2.15	<0.001(HS)
1vs4	0.11	0.695(NS)
2vs3	0.97	0.540 (NS)
2vs4	1.29	<0.001(HS)
3vs4	2.26	<0.001(HS)

Observations table 3: Intra-group comparison of amplitude of motor nerves (CMAP) shows no significant difference in light smokers as compared to non-smokers. Also there is no significant difference in the amplitude of motor nerves among moderate & heavy smokers. When amplitudes of light smokers are compared with moderate & heavy smokers, the difference is highly significant. Moderate & heavy smokers also showed significant difference when compared with non-smokers.



Bar Diagram 1C showing distal Latency

Table 4: Tukey's Post Hoc Analysis for Intra-group comparison of Distal latency

Groups	MEAN DIFFERENCE	P VALUE
1 vs 2	-.21000*	<0.001(HS)
1vs3	-1.74200*	<0.001(HS)
1vs4	.23500*	<0.001(HS)
2vs3	-1.53200*	<0.001(HS)
2vs4	.44500*	<0.001(HS)
3vs4	1.97700*	<0.001(HS)

Observations Table 4:
Intra-group comparison of distal latency shows highly significant difference in smokers as compared to smokers as well as among all the groups.

DISCUSSION

Motor nerve conduction velocity (MNCV) and CMAP- Compound Muscle action potential (amplitude) of peripheral motor nerves in both upper & lower limbs are significantly reduced in smokers as compared to non-smokers while distal latency of peripheral motor nerves is highly significantly prolonged in smokers as compared to non-smokers.

Another important observation is that conduction velocity is lowest and distal latency is prolonged more in heavy smokers. Hence, the results reveal the dose response relationship.

Tukey's post hoc analysis for intra-group comparison of MNCV shows difference in the mean values of MNCV among light, moderate & heavy smokers are not significant. When results are compared with the non-smokers, highly significant decrease in MNCV values are seen in light, moderate & heavy smoker groups.

Conduction velocity depends on the amount of myelination to the nerve fiber available. Direct toxicity of nicotine or hypoxemia may damage myelin sheath resulting in reduced conduction velocity.

Intra-group comparison of amplitude of motor nerves (CMAP) shows no significant difference in light smokers as compared to non-smokers. Also there is no significant difference in the amplitude of motor nerves among moderate & heavy smokers But when amplitudes of light smokers are compared with moderate & heavy smokers, the difference is highly significant. Moderate & heavy smokers also showed significant difference in the amplitude when compared with non-smokers.

The amplitude of CMAP represents the summated action potentials from each of the muscle fibers supplied by their respective nerve fibers, indirectly depends on the number of available nerve fibers supplying them. But significant re-innervation of the denervated muscle fiber occurs by the adjacent viable nerve fiber. This is probably why CMAP amplitude is maintained in light smokers and axonal loss is not significant, Intra-group comparison of distal latency shows highly significant difference in smokers as compared to non-smokers as well as among all the groups which means demyelination starts early in the nerves of smokers further progressing to axonal or mixed degeneration type of neuropathic changes.

Motilal C.Tayade, et al[9] in 2012 stated that Statistically significant changes ($P < 0.05$) were found in the sensory nerve conduction velocity (Mean+ SD value in smokers was 55.11+ 2.32 m/s while in nonsmokers it was 57.09+ 4.21 m/s) whereas no such changes were found in Motor nerve conduction velocity (Mean+ SD value in smokers was 54.19 +6.35 m/s while in nonsmokers it was 54.97+ 7.33 m/s) in this study.

In our study, in heavy smokers, we found statistically significant dysfunction in motor nerves conduction study.. The damage to peripheral motor nerves not found in the above study could be due to the age group taken in the above study which was 25-40 years which means maximum duration of smoking was just 20 years (15 plus history of 5 years smoking) while in our study the age group of subjects was from 20-40 plus history of 5 years of smoking which is equal to 25 years. This can also be concluded that motor nerves are affected later than sensory nerves due to smoking. Damage to peripheral motor nerves may need greater exposure to smoking resulting in more toxicity and more hypoxemia.

Cigarette smoking affects neural function by various mechanisms. Smoking causes vasoconstriction and damages blood vessels by atherosclerosis, plaque formation etc. As a result the blood supply and amount of oxygen delivery to the nerve fibers decreases. (neural ischemia) Smoking also increases cholesterol level in the circulating blood stream which predisposes to the atherosclerosis.The body's overall vascular and neural functions are closely related. The initial change which occurs as a result of smoking is constriction of microvasculature. Such microvascular function impairment occurs early in smoking. Hence smoking affects peripheral ends of nerves and then slowly proceeds towards the centre[9]. Carbon monoxide released during smoking also damages tunica intima of blood vessels and endothelial cells, which further leads to deposition of fats in the vessel walls. Nicotine present in smoke worsens these effects[10].

Myelin, forming a layer around the axon , is essential for the normal functioning of the nervous system. Smoking initially induces subclinical changes in the myelin sheath.This results in demyelination . This can also cause the blockage of the nerve conduction and decrease in conduction velocity.Also the higher carboxyhemoglobin levels in the circulating blood found in smokers leads to slowing of nerve conduction by its direct action over the myelin sheath. Nicotine too has a direct effect on the myelin sheath. In clinical practice, a high frequency of neuropathies of different varieties has been reported in more than 60 percent smokers.[9]

In our study, all the values of MNCS & SNCS are within normal values[11] but when they are compared to the value of non-smoker group, they are highly significantly reduced. An important fact about the study is that all the cases showing dysfunction are subclinical in nature because symptomatically the smokers did not complain of any signs of nerve involvement. This finding is in line with the studies by **Agrawal D et al**[12] who also found sub-clinical neuropathy in stable COPD patients.

Our findings make strong background for the future neuropathic changes as observed by different authors in COPD patients. Hence it can be concluded from the above finding that long before the appearance of clinical neuropathy, the deterioration in nerves can be diagnosed earlier by electrophysiological studies.

Summary and Conclusion

NCV values are within normal range among smokers but statistically all the values of MNCV are significantly reduced as compared to the non-smokers which means neural dysfunction starts in early years of smoking. NCS study also shows dose response relationship in smoking. More the smoking Index, more is the dysfunction in peripheral nerves. All the cases of neural dysfunction are sub-clinical in nature. These results make a strong foundation for future neuropathic changes in apparently healthy adult male smokers as observed in different studies in COPD patients. Further studies are needed to confirm the findings in smokers with larger sample size.

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