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Original Article

Physiology Section

Nerve Conduction Velocity in Smokers and Gutka Chewers: A Case-control Study

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ABSTRACT

Introduction: Chemicals that are present in cigarette/bidi smoke and gutka have been known to cause subclinical changes in myelin sheaths of peripheral nerves. Despite the antiquity and popularity of smoking and gutka chewing, its effect has not been investigated systematically in young adults.

Aim: To investigate the chronic effects of smoking and gutka chewing on Nerve Conduction Velocity (NCV).

Materials and Methods: The case-control study was conducted in the Department of Physiology, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh, India, from November 2018 to December 2020. A 40 male smokers (age group 20-60 years), 40 gutka chewers (age group 20-60 years) along with 40 age matched healthy male controls. The nerve conduction study was performed by using fully computerised Electromyography (EMG) and NCV machine. Sensory Nerve Conduction Velocity (SNCV) and Motor Nerve Conduction Velocity (MNCV) test of median and ulnar nerves was performed on subjects. Data was analysed by using unpaired t-test.

Results: In this study of comparative analysis of total 120 subjects, [40 controls and 80 cases (40 cases of smokers and tobacco chewers each)], statistically significant changes (p-value <0.05) were found in the sensory NCV of both the nerves and motor NCV of median nerve in smokers whereas no such changes were found in motor NCV of both nerves in gutka chewers.

Conclusion: It can be concluded that smoking causes more reduction in NCV than gutka chewing.

Keywords: Electromyography, Median nerve, Tobacco, Ulnar nerve

INTRODUCTION

India is among the world's top five tobacco producers and consumers. The World Health Organisation (WHO) attributed 4 million tobacco related death every year and is expected to rise by 8 million death by 2020 [1]. Two major form of tobacco use in India are smoking and chewing [2]. Guthka is industrially prepared smokeless tobacco most commonly available in India, Pakistan and South east Asian countries. Near about 4200 different chemical constituents have been identified in gutka [3]. The main carcinogens that are present in gutka are mainly derived from its constituents including areca nut, tobacco, slaked lime and catechu [4].

Smoke of cigarette/bidi possess a significant health hazard to human beings, especially affecting the haemodynamic of cardiovascular and cause involvement of more than one system of body. Chemicals present in cigarette/bidi smoke like nicotine, tar, carbon monoxide, tar, oxidative gases, polycyclic aromatic hydrocarbons, carbonyls, butadiene, metals, carbon disulphide and benzene etc., have been shown to cause subclinical changes in myelin sheaths of peripheral nerves and results in demyelination which causes poor electrotonic nerve conduction [5]. This may cause nerve dysfunction particularly in the form of decreases in NCV. Chronic hypoxaemia caused by prolonged tobacco exposure cause negative effect on nerves, which results in peripheral neuropathy [6].

Nerve conduction velocity is considered as the most commonly used methods to study the peripheral nerves because of their accuracy in diagnosing conditions related to nerve. It is also helpful is differentiating between the true nerve disorder and conditions which are affected by injury of nerves. Peripheral nerves, that is, ulnar and median nerves in upper extremity are most commonly chosen for NCV as they are easily reachable [7].

There are studies that evaluated only the effect of smoking on NCV, and there is no study till date assessing the effect of gutka chewing. Hence, the present study was conducted with an aim to evaluate the effect of smoking and gutkha chewing on nerve conduction study.

MATERIALS AND METHODS

The case-control study was conducted in the Department of Physiology, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh, India, on smokers and gutkha chewers from November 2018 to December 2020. This study was approved from the Ethical Committee (Letter no. 249) of JN Medical College.

Total 120 sample subjects were taken- 40 as control and 80 as cases. A detailed history and physical examination was carried out for every subject who entered the study as per a designed proforma and the selected cases of smoking and gutka chewing, between were assessed for NCV. They were advised for neuropathy assessment and were asked to report in neurophysiology laboratory after an overnight abstinence of smoking and gutka chewing.

All the cases (80) were divided in two groups:

Group 1 (n=40) smokers,

Group 2 (n=40) gutkha chewers

and another 40 age matched male healthy controls were taken for proper comparative analysis. They were free from any other illness which could hamper with the test results.

Inclusion criteria: Only male smokers and gutka chewers aged between 20-60 years, who came to the chosen study centre during the study time period were included in the study as case groups.

Those healthy age matched volunteers from the general population who were interested in participating in the study during the given time period were included as control group.

Exclusion criteria: Those patients who came to the study centre with hypertension or with any other obvious cause of neuropathy e.g., alcohol abuse, vitamin B12 deficiency, neuropathies associated with exogenous toxic agents, metal or drugs and those patients with history of trauma in the course of nerve to be examined were excluded from the study.

Assessment of Peripheral Neuropathy

Nerve Conduction Velocity Test

Sensory Nerve Conduction Velocity (SNCV): The sensory conduction was measured orthodromically and antidromically. In orthrodomic

conduction study, a distal portion of the nerve, e.g., digital nerve was stimulated and Sensory Nerve Action Potential (SNAP) was recorded at a proximal point along the nerve. In antidromic conduction study, the nerve was stimulated at a proximal point and SNAP is recorded distally. In the present study, sensory nerve action potential was recorded antidromically.

Stimuli were supramaximal and of 0.1 ms duration at a frequency of 1 Hz. The filter setting for sensory conduction were 20 Hz-3 KHz, sweep speed was 2 ms/division. The signal enhancement for averaging is generally required for sensory conduction study. The signal enhancement with averaging is proportional to the square root of the number of trials [Table/Fig-1].

Change in amplitude=√n; where 'n' is the no. of trials

Nerve	Antidromic/Orthro	Stimulated site	SNAP recorded form
Median	Antidromic	Wrist	Index finger
Ulnar	Antidromic	Wrist	Little finger

[Table/Fig-1]: Sensory Nerve Conduction Velocity (SNCV).
SNAP: Sensory nerve action potential

The onset latency of the potential was measured from the stimulus artifact to the initial negative peak. SNCV unlike MNCV was measured by stimulating at a single stimulation site, because the residual latency which comprises neuromuscular transmission time and muscle propagation time is not applicable in sensory nerve conduction. Thus, the SNCV is calculated by dividing the distance (mm) between the stimulating and recording sites by the latency (ms). SNCV=Distance/Latency(m/s)

Motor nerve conduction velocity: The motor or mixed nerve was stimulated at two points along its course as shown in [Table/Fig-2]. The stimulation intensity was adjusted to record a Compound Muscle Action Potential (CMAP). Stimulation intensity was increased gradually and the point at which the amplitude did not increase any further was determined as the supramaximal intensity. This was the intensity at which the response was recorded. The duration of stimuli was 0.1 ms. The cathode of the stimulator was kept close to the active electrode. The surface recording electrode were used and placed in belly tendon montage; keeping the active electrode close to the motor point and the reference to the tendon. Ground electrode was placed between the stimulating and the recording electrodes. A biphasic action potential with initial negativity was thus recorded.

Nerve	Distal site of stimulation	Proximal site of stimulation	CMAP record from:
Median	Wrist	Antecubital fossa	Median Wrist Antecubital fossa Ulnar Wrist Elbow
Ulnar	Wrist	Elbow	Abductor Digiti Minimi (ADM)

[Table/Fig-2]: Motor Nerve Conduction Velocity (MNCV).
CMAP: Compound muscle action potential

Calculation of MNCV: The onset latency is the time in millisecond from the stimulus artifact to the first negative deflection of CMAP. MNCV was calculated by measuring the distance in mm between the two point of stimulation, which was divided by latency difference between the proximal and the distal latencies (ms). The NCV is expressed as m/s.

MNCV=D/{(PL-DL)} (m/s)

where, PL is the proximal Latency (ms); DL is the Distal Latency (ms); D is the distance between proximal and distal stimulation sites (mm).

STATISTICAL ANALYSIS

Descriptive statistic were used for analysis of the data.

RESULTS

There was no significant difference in the age between cases and control group in smokers and gutkha chewers [Table/Fig-3].

Parameter	Smokers in case group (n=40) (Mean±SD)	Gutka chewers in case group (n=40) (Mean±SD)	Control group (n=40)	p-value*
Age (years)	40.22±8.10[a]	38.25±7.84[b]	38.32±6.44[c]	0.10[ac], 0.47[bc]

[Table/Fig-3]: Comparison of age in cases and control group. Smokers (n=40), Gutkha chewers (n=40) and control subjects (n=40).
(Independent t-test for unpaired samples was applied); a: Mean age of the smokers ; b: Mean age the of the Gutka Chewers; c: mean age of control subjects; ac: p-value denotes comparative analysis between age of smokers and that of control group subjects. bc: p-value denotes the comparative analysis between age group of Gutka chewers and that of the control group subjects

NCV parameters: A significant bilateral decrease was observed in MNCV of the median nerve as compared to the control subjects. No significant decrease seen in MNCV of ulnar nerve [Table/Fig-4].

Parameters	Smokers in case group (n=40) Mean±SD	Control (n=40) Mean±SD	p-value
Right median velocity (ms)	53.86±4.56	57.46±2.60	<0.05*
Left median velocity (ms)	54.97±3.79	56.88±3.03	<0.05*
Right ulnar velocity (ms)	56.98±3.68	57.09±3.03	0.31
Left ulnar velocity (ms)	55.67±4.10	57.36±1.85	0.30

[Table/Fig-4]: Comparison between Motor Nerve Conduction Velocity (MNCV) of median and ulnar nerve in smokers (n=40) and control group (n=40).
(Independent t-test for unpaired samples was applied); *p-value <0.05: Statistically Significant

No significant decrease was observed in the MNCV of right median, left median, right ulnar and left ulnar velocity in gutka chewers as compared to control group [Table/Fig-5]. A significant bilateral decrease was observed in the SNCV of median and ulnar nerve in smokers as compared to control group [Table/Fig-6].

Parameters	Gutka chewers in case group (n=40) Mean±SD	Control (n=40) Mean±SD	p-value
Right median velocity (ms)	55.40±4.54	57.46±2.60	0.41
Left median velocity (ms)	56.15±3.89	56.88±3.03	0.10
Right ulnar velocity (ms)	56.99±4.36	57.09±3.03	0.3
Left ulnar velocity (ms)	55.54±3.19	57.36±1.85	0.22

[Table/Fig-5]: Comparison between Motor Nerve Conduction Velocity (MNCV) of median and ulnar nerve in gutka chewers (n=40) and control group (n=40).
(Independent t-test for unpaired samples was applied); *p-value <0.05: Statistically significant

Parameters	Smokers in case group (n=40) Mean±SD	Control (n=40) Mean±SD	p-value
Right median velocity (ms)	51.22±4.08	55.94±3.02	<0.01*
Left median velocity (ms)	52.73±4.96	56.55±2.21	<0.01*
Right ulnar velocity (ms)	51.97±5.03	56.36±3.10	<0.01*
Left ulnar velocity (ms)	52.26±4.49	55.85±2.68	<0.01*

[Table/Fig-6]: Comparison between Sensory Nerve Conduction Velocity (SNCV) of median and ulnar nerve in smokers (n=40) and control group (n=40).
(Independent t-test for unpaired samples was applied); *p-value <0.05: Statistically Significant

A significant bilateral decrease was observed in SNCV of right and left median and ulnar nerve in gutka chewers as compared to control group [Table/Fig-7].

Parameters	Gutka chewers in case group (n=40) Mean±SD	Control (n=40) Mean±SD	p-value
Right median velocity (ms)	52.99±4.83	55.94±3.02	<0.05*
Left median velocity (ms)	54.73±4.98	56.55±2.21	<0.05*
Right ulnar velocity (ms)	53.99±4.42	56.36±3.10	<0.05*
Left ulnar velocity (ms)	53.78±4.92	55.85±2.68	<0.05*

[Table/Fig-7]: Comparison between Sensory Nerve Conduction Velocity (SNCV) of median and ulnar nerve in gutka chewers (n=40) and control group (n=40).
(Independent t-test for unpaired samples was applied); *p-value <0.05: Statistically significant

DISCUSSION

From the study, it is seen that statistically significant changes were found in conduction velocity of sensory nerves and motor nerves. Nerve conduction studies provide a means of demonstrating the

presence and extent of a peripheral neuropathy [8]. Conduction velocity is usually reduced in demyelinative neuropathies, including smoking. NCV tests can precisely measure the degree of damage in large nerve fibres like median nerve, revealing whether symptoms are being caused by degeneration of the myelin sheath [9]. In the present study, the authors recorded sensory and motor conduction velocities using surface electrodes which require less precision in placement and are therefore quicker to use. Uncertainty of exact site of stimulation, lack of precision of measured conduction distance and uncertainty as to the temperature of the nerve can introduce errors in velocity measurements [10]. By using computerised technique, majority of these errors can be eliminated giving more reliable and reproducible results. The conduction velocity values found in this study are seen similar to those observed by Agrawal D et al., who studied subclinical peripheral neuropathy in chronic obstructive pulmonary disease patient [11]. 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. Smoking also increases the level of cholesterol in the circulating blood stream which predisposes to the atherosclerosis [12]. The initial change which occurs as a result of smoking is constriction of microvasculature. Such microvascular function impairment occurs early in smoking.

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 [13]. The layer of myelin around the axon is essential for the normal functioning of the nervous system [14]. During the initial period, smoking brings about subclinical changes in the myelin sheath that finally progresses into demyelination [15]. Due to the demyelination, nerve conduction blocks and the conduction velocity decreases [16]. Besides, the carboxyhaemoglobin formed in blood of smokers also decreases nerve conduction [17].

Gutka contains nicotine and known carcinogenic chemicals such as tobacco-specific A-nitrosamines, lime, catechu, betel nut, benzopyrene, nitrate, cadmium, lead, arsenic, nickel, and chromium [18,19]. Nicotine is the active ingredient in gutka and is readily absorbed from the respiratory tract, buccal mucous membrane, and the skin. Approximately, 80-90% altered in the body, mainly in the liver and also in the kidney and the lungs [20]. Nicotine and lime both cause degeneration of myelin sheath by producing reactive oxygen species.

In the present study, there were more statistically significant changes in SNCV, this may be due to the fact that sensory nerves are thinner than the motor nerves and are having shorter internodal distances. As a result, the thinner nerves are early affected than the thicker nerves by any damage. Hence, the sensory nerves are more affected than the motor nerve [21]. Further in this study, it was also found that more severe changes in SNCV in smokers than gutka chewers. This may be due to fact that smoking causes decrease in conduction velocity by generating free radicals, by increasing the level of cholesterol as compared to gutka chewing.

Limitation(s)

The limitations of the study is its small sample size.

CONCLUSION(S)

On assessment of peripheral neuropathy through sensory and motor nerve conduction study, it was seen that conduction velocity was decreased in both smokers and gutka chewers, showing the involvement of sensory nerves in gutka chewers and both sensory and motor nerves in smokers. There was also early involvement of sensory nerves in both groups.

These results make a strong foundation for future neuropathic changes in apparently healthy adult male smokers and gutka chewers as observed in different studies in Chronic Obstructive Pulmonary Disease (COPD) patients. Further studies are needed to confirm the findings with larger sample size.

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