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RESEARCH ARTICLE

Influence of cigarette smoking on human cardiovascular sympathetic autonomic functions

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ABSTRACT

Background: From analytical and statistical studies, it has been firmly concluded that cigarette smoking has various hazards on different systems of human being. **Aims and Objectives:** The aims and objectives of this study were to determine cardiovascular sympathetic activity in habitual cigarette smokers and compare it with healthy age-matched controls and to find out any correlation between duration of cigarette smoking and sympathetic dysfunction. **Materials and Methods:** This study was conducted in 40 habitual cigarette smokers (study group) and 40 normal, healthy nonsmokers (Control group) who served as age-matched controls to study sympathetic functions. The participants were in the age range of 20-45 years. The participants were selected from the habitual cigarette smoking (10-25 cigarettes/day) and nonsmoking students and employees in the medical college campus by convenience sampling method. Following the basal recording of physiological and sympathetic function parameters, the participant was required to smoke 1 full cigarette within 5 min at his usual puffing rate. 5 min after the participant completed to smoke the cigarette, the autonomic function parameters are again recorded. Blood pressure (BP) response to orthostatic test and to sustained handgrip exercise. The data were suitably arranged and were subjected to statistical analysis; the level of significance is calculated by applying *t*-test. **Results:** Significant raise in diastolic BP after cigarette smoking in the study group. **Conclusion:** Habitual smoking affects negatively the sympathetic autonomic nervous system.

KEY WORDS: Blood Pressure; Cigarette Smoking; Hand Grip Dynamometer; Sympathetic Nervous System

INTRODUCTION

The autonomic nervous system controls smooth muscles, cardiac muscle, and glands (both endocrine and exocrine). The organs innervated by the autonomic nervous system have an intrinsic activity of their own. Autonomic innervations only serve to modulate the activity of these organs as per the needs.[1] The autonomic nervous system is governed centrally by brain stem centers; hypothalamus, cerebellum, frontal cortex, and limbic system. Hypothalamus is the most important; in fact, Sherrington rightly called it as "Head Ganglion of the autonomic nervous system." The sympathetic division in addition to subserving basic functions as maintenance of blood pressure (BP) and body temperature helps the individual to cope with the emergencies. Sympathetic stimulation leads to relaxation of accommodation and dilatation of pupils, acceleration of heartbeat, increase in BP, increase blood flow to muscles and decreased blood flow to skin and abdominal viscera, elevated plasma glucose and free fatty acid levels. On the basis of these effects, Cannon called this emergency reaction as "preparation for flight or fight."[2]

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Cardiovascular effects of smoking in man and experimental animals are those caused by nicotine alone. A smoker who inhales gets usually 0.1-0.2 mg nicotine/inhalation and 1-2 mg from single cigarette. The effects of nicotine on the cardiovascular system are resultant of number of actions on several components of systems. Low concentration of nicotine stimulates sympathetic ganglia and high concentration paralyzes them. The parasympathetic ganglia respond in same way but in less sensitive manner. Nicotine is classically considered an agonist at nicotinic receptors at the level of autonomic ganglia and neuromuscular junction of skeletal muscle.[3] In certain circumstances nicotine also exhibits nicotinic blocking properties;[4] therefore, the effect of nicotine will vary depending on dose and route of administration. Nicotine promotes release of Epinephrine from adrenal gland and other chromaffin tissue and norepinephrine from hypothalamus and adrenergic synapses. Physiological effects of smoking on the cardiovascular system are alteration in heart rate, rhythm, BP, cardiac output, myocardial oxygen and nutrient demand, peripheral vascular resistance, ventricular fibrillation threshold, and coronary artery flow regulation.

Hence, this study was planned with the following objectives: (i) To determine cardiovascular sympathetic activity in habitual cigarette smokers and compare it with healthy age-matched controls and (ii) to find out any correlation between duration of cigarette smoking and sympathetic dysfunction.

MATERIALS AND METHODS

It was an experimental study design. The study was approved by the Institutional Ethical Committee. This study was conducted in 40 habitual cigarette smokers (study group) and 40 normal, healthy non-smokers (control group) who served as age-matched controls to study sympathetic autonomic functions as given below. The participants were in the age range of 20-45 years. The participants were selected from the habitual cigarette smoking (10-25 cigarettes/day)[5] and non-smoking students and employees in the medical college campus by convenience sampling method. Each participant in study and control groups taking part was explained about the procedure to be adapted in the research. All the participants after thoroughly understanding the procedures to be adapted signed an informed consent form provided to them by the investigator. All the participants underwent a thorough clinical examination.

The participants without signs of cardiovascular, endocrinological, neurological, hematological, and inflammatory diseases were selected for the study. While, the participants with any of the following findings were excluded from the study: (i) Evidence of hypertension (systolic BP [SBP] ≥140 and diastolic BP [DBP] ≥90 mmHg); (ii) clinical signs of cardiac failure or electrocardiogram changes suggestive of arrhythmia, ischemia; (iii) participants having, diabetes mellitus, bronchial asthma, giddiness on standing, syncopal spells, visual disturbances, nocturnal diarrhea; (iv) participants receiving drugs that are known to interfere with cardiac or respiratory functions such as beta blockers, sympathomimetic drugs, antihypertensive drugs, vasodilators, and diuretics; (v) participants having diseases or conditions known to affect autonomic function such as Guillain–Barre syndrome, poliomyelitis, diphtheria, tuberculosis, syphilis, amyloidosis, and chronic renal failure; (vi) participants having history of alcohol consumption, chronic tobacco consumption in any other form; (vii) study participants who smoke <12 cigarettes/day.

History related to cigarette smoking was taken in detail in regard to number of cigarettes/beedis smoked/day, duration of smoking in years and whether full length of cigarette got smoked or partial smoking. Sphygmomanometer and hand grip dynamometer were used apart from the instruments used for the anthropometric measurements.

Methodology

All the selected participants were asked to come to the Research Laboratory of Department of Physiology at 8.30 am. The participants were instructed to come on empty stomach with overnight abstinence from smoking, coffee, and tea or any form of exercise. All the tests were conducted between 8.30 am and 11.00 am in cool and calm atmosphere at room temperature varying from 27°C to 30°C. The participants were asked to relax in supine position for 30 min in the laboratory; tests were performed only after complete relaxed physical and mental state of the participant. All the participants were subjected to recording of their physical anthropometry, various physiological parameters, and autonomic function parameters.

Following the basal recording of physiological and sympathetic autonomic function parameters in study participants, the participant was required to smoke 1 full cigarette (Gold Flake Kings, ITC Ltd.) within 5 min at his usual puffing rate. 5 min after the participant completed to smoke the cigarette, the sympathetic autonomic function parameters are again recorded.

For each participant (both study and control groups), the following anthropometric parameters were recorded: (i) Height (in cm): This was measured with participant standing without his shoes, nearest to 0.1 cm; (ii) weight (in kg): The participants were weighed in standardized machine with minimum of their clothing's, nearest to 0.1 kg; (iii) body surface area (m^2): This was calculated in each participant by using Dubois nomogram; (iv) body mass index (kg/m^2): This was calculated for each participant from his height and weight.

In each participant, the following physiological parameters: (i) Respiratory rate (cycles per minute); (ii) heart rate (beats per minute); (iii) SBP and DBP (mmHg) by using mercury sphygmomanometer.

The sympathetic autonomic nervous function tests were selected as recommended by American Diabetic Association and performed as per methods described by Bannister:[6] (i) BP response to orthostatic test: The participant rested comfortably in supine position for 15 min, and then the participant was asked to stand up unaided and remain standing. SBP was recorded in resting supine position and again immediately when he stands up. Moreover, the difference in SBP was noted. And (ii) BP response to sustained handgrip exercise: The participant was asked to sit comfortably in chair. Initially, the participant was asked to exert maximal hand grip strength on hand grip dynamometer with dominant hand. First, the maximum voluntary contraction (MVC) is determined and then the participant was then asked to exert 30% of MVC for 5 min (at least for 3 min) with dominant hand. DBP was measured in the non-dominant hand at rest and at 1 min intervals during hand grip. The maximum rise in DBP during 30% of MVC over the resting DBP was noted. Grading[7] and autonomic function score[8] of the results:

Score	0 (Normal)	1 (Borderline)	2 (Abnormal)
BP response to standing	<10 mmHg	11-29 mmHg	>30 mmHg
BP response to sustained hand grip	>16 mmHg	11-15 mmHg	<10 mmHg

BP: Blood pressure

Statistical Analysis

The data were suitably arranged and were subjected to statistical analysis; the level of significance is calculated by applying *t*-test. All the values are expressed in mean ± standard error of mean. The results were expressed as nonsignificant if $P > 0.05$, significant if $P < 0.05$, highly significant $P < 0.01$ and very highly significant if $P < 0.001$.[9] Correlation and regression were used to examine the strength of association before smoking with duration of smoking.

RESULTS

Anthropometric parameters were recorded in participants of both groups and described in Table 1. According to Table 1, there is no significant difference found between control and study groups in all anthropometric parameters. Baseline physiological parameters were recorded in participants of both groups and described in Table 2. There was no significant difference found between control and study groups in heart rate, respiratory rate, and SBP. However, baseline DBP was found to be more in study group, and the difference was found to be statistically significant (P <0.05).

Table 3 shows the effect of change in BP in response to standing and in response to sustained handgrip in control and in study groups before smoking. There was no significant difference found between the groups in terms of change in BP. There was high significant difference was found in change in DBP in response to sustained handgrip between in control and study groups after smoking ($P = 0.002$) (Table 4). A significant difference was also found in change in DBP in response to sustained handgrip between in study group before and after smoking ($P = 0.029$) (Table 5).

DISCUSSION

BP response to orthostatic test; with change of posture from supine to standing the autonomic nervous system acts to

Table 1: Anthropometric parameters recorded in participants of different groups (n=40 in each group)

Parameters	Control group	Study group	*P* value
Age (years)	30.00±1.34	26.70±1.3	0.092
Height (cm)	168.15±0.980	168.22±0.973	0.957
Weight (kg)	61.07±1.454	61.07±1.578	1.000
BSA (m^2)	1.45±0.05	1.49±0.09	0.962
BMI (kg/m^2)	21.24±3.75	21.02±2.12	0.860

Values are expressed in mean±SEM. BSA: Body surface area, BMI: Body mass index, SEM: Standard error of mean

Table 2: Physiological parameters recorded in participants of different groups (n=40 in each group)

Parameters	Control group	Study group	*P* value
Heart rate (/min)	76.55±1.567	75.75±1.349	0.700
Respiratory rate (/min)	18.17±0.494	18.15±0.302	0.966
SBP (mmHg)	107.25±1.484	110.45±1.704	0.161
DBP (mmHg)	72.95±1.322	76.70±1.08	0.031*

Values are expressed in Mean±SEM. *P<0.05: Significant, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SEM: Standard error of mean

Table 3: Sympathetic autonomic function parameters of participants in study (before smoking) and control group (n=40 in each group)

Sympathetic autonomic function parameters	Study group before smoking	Control group	*P* value
BP response to standing (fall in SBP)	10.80±0.958	11.25±0.593	0.691
BP response to sustained hand grip (increase in DBP)	26.4±1.043	23.75±1.259	0.109

Values are expressed in Mean±SEM. SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SEM: Standard error of mean, BP: Blood pressure

Table 4: Sympathetic autonomic function parameters of participants in study (after smoking) and control group (n=40 in each group)

Sympathetic autonomic function parameters	Study group after smoking	Control group	*P* value
BP response to standing (fall in SBP)	11.02±0.904	11.25±0.593	0.836
BP response to sustained hand grip (increase in DBP)	29.3±1.210	23.75±1.259	0.002**

Values are expressed in mean±SEM. SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SEM: Standard error of mean, BP: Blood pressure

Table 5: Sympathetic autonomic function parameters of participants in study (before and after smoking) (n=40)

Sympathetic autonomic function parameters	Before smoking	After smoking	*P* value
BP response to standing (fall in SBP)	10.80±0.958	11.02±0.904	0.844
BP response to sustained hand grip (increase in DBP)	26.4±1.043	29.3±1.210	0.029*

Values are expressed in mean±SEM. *P<0.05: Significant, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SEM: Standard error of mean, BP: Blood pressure

produce a rise in heart rate and vasoconstriction to maintain BP.[10] Vasoconstriction is mediated through sympathetic innervations to blood vessels during standing. In our study, there was no significant fall in BP after standing from supine posture in control and study groups before and after smoking the cigarette. Our observation is in agreement with the observations of Marshall et al.,[11] and Lucini et al.[12]

Lucini et al. attributed this to stimulation by nicotine receptors located at a central, ganglionic or peripheral level, including sensory endings of afferent fibers such as those innervating the lungs and their circulation which might be capable of initiating pressor sympathetic reflexes.

Davis et al.[13] found a fall in SBP in hypertensive smokers. Baroreceptors of hypertensives are not as responsive as those of normal and that decreased arterial wall compliance is the mechanism of decreased baroreceptor responsiveness in arteriosclerosis and in hypertension.

BP response to sustained handgrip exercise; Ewing et al. (1974)[14] first showed that during sustained handgrip, there was a sharp rise in DBP due to increase in peripheral vascular resistance. The results of this study revealed a significant rise in BP in smokers as compared with non-smokers. This is in accordance with the study conducted by Humphreys and Lind,[15] Tucci and Sode,[16] Cryer et al.,[17] Benowitz et al.,[18] Niedermaier et al.,[19] Grassi et al.,[20] Kotamäki,[21] and Gerhardt et al.[22] The study of comparison with smokers and nicotine gums conducted by Benowitz et al.[18] concluded that prominent cardiovascular effects of nicotine were a result of activation of the sympathetic nervous system because of which smoking increases heart rate and BP. The cause of increase heart rate and BP in our study may be due to the same mechanism. Grassi et al.[20] in their study to understand mechanism responsible for sympathetic activation by cigarette smoking in human opined the pressor and tachycardic effects of cigarette smoking are associated with plasma catecholamines suggesting an adrenergic stimulation. In our study, there is an increase in BP in smokers over non-smokers which could be explained due to increased sensitivity of sympathetic nervous system due to the stimulating tests (sustained hand grip) and requires further study. In 1999, Gerhardt et al.[22] studied effects of smoking on baroreceptors in smokers more than 6 years. According to their study, smoker showed increased BP than non-smokers. These findings are same as per our results. Tucci and Sode[16] studied effects of smoking upon adreno-cortical and sympatho-medullary activity in 94 males. According to their study, there is no change in pituitary adrenocortical and sympatho-medullary activity. However, our results suggest that smoking increased sensitivity of sympathetic nervous system. The variation in the results was because they had not performed any stimulation test, which was conducted in our study (sustained hand grip test). Laustiola et al.[23] showed that long-term smoking induces downregulation of beta adrenergic receptors, though plasma catecholamine levels were significantly higher in smokers than non-smokers as explained by beta blockers which were less effective in the treatment of hypertension in smokers as compared with non-smokers. Their observations indicate that cigarette smoking might induce a beta adrenergic tone with considerable impact on cardiovascular regulations. Further, these results implied even if beta receptor function per se unaltered in cigarette smokers their down regulation of beta receptor may result in relative increase in alpha-adrenergic tone at any given catecholamine concentration. In our study, during handgrip test, the rise in BP was higher in smokers over non-smokers may be explained on the basis of increased alpha-adrenergic tone leading to vasoconstrictive tendency of blood vessels, due to increased sensitivity of sympathetic nervous system.

Thus, our observations reveal that there is increase in basal diastolic pressure in habitual smokers which is statistically significant when compared to age-matched controls. Furthermore, there was a significant change in heart rate response during deep breathing indicating change in parasympathetic activity. During BP response to handgrip exercise, there is a significant increase in DBP indicating affection of sympathetic nervous system. Autonomic function score indicates the autonomic dysfunction. More autonomic function score is observed in smokers before and after smoking which is due to more parasympathetic dysfunction than sympathetic. Further the results of autonomic function

score when compared for the duration of exposure, we found there was a minor degree of correlation between autonomic function scores and duration of cigarette smoking.

CONCLUSION

Thus, we conclude that habitual cigarette smoking affects both parasympathetic system and sympathetic nervous system. The knowledge about the status of the autonomic nervous system with cigarette smoking will be useful in the management of cardiovascular disturbances. The alteration of autonomic balance with cigarette smoking will also have a bearing on drug action and in determining therapeutic strategy in habitual smokers. We feel that further research should be focused in this field at fundamental level and insights gained from these studies should be applied.

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