

## Study of autonomic functions in cigarette smokers

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### Abstract

**Introduction:** Smoking is one of the most ancient and widespread man's activities. The present study was chosen to determine sympathetic and parasympathetic activity in cigarette smokers and compare it with healthy age matched controls in order to find out what influence does smoking have on baroreceptor sympathetic and parasympathetic control mechanisms and to find out for any co-relation between duration of cigarette smoking and autonomic dysfunction.

**Materials & Methods:** Fifty cigarette smokers and fifty normal, healthy, nonsmokers were selected as age matched controls to study autonomic functions. Sympathetic functions were carried out by Cold Pressor Response test and Hand Grip test. Parasympathetic functions were tested by Determination of Heart Rate with change in posture and Sinus Arrhythmia.

**Results:** Smokers revealed more pronounced rise both in systolic as well as diastolic blood pressure as compared to normal healthy controls during cold pressor test. Smokers revealed more pronounced rise in both SBP and DBP as compared to nonsmokers during hand grip test. There was increased heart rate in initial 10 seconds when there is postural change i.e. lying down to standing in both the groups. There was an increase in heart rate during inspiration and decrease during expiration (sinus arrhythmia) both in smokers and healthy controls.

**Conclusion:** Cigarette smoking affects cardiovascular functions as indicated by rise in blood pressure in smokers than nonsmokers reflects the sensitivity of sympathetic activity to nicotine due to smoking. Thus the study concludes that smoking possibly has an effect on neurocardiovascular regulation system altering the sensitivity of ANS activity in habitual smokers.

**Keywords:** Autonomic Function Tests, Smokers, Non-smokers, Cold Pressor Test, Hand Grip Test, Heart Rate.

### 1. Introduction

In 1988, Langley wrote I propose the term "Autonomic Nervous System" for sympathetic nervous system of cranial and sacral nerves and for the local nervous system of the gut[1]. The term did not gain general acceptance at first and Gaskell called "Involuntary Nervous System" in his book published in 1916[2]. However passage of time has favored Langley and today the autonomic nerves are generally regarded as motor nerves of sympathetic and parasympathetic system. Autonomic nervous system consists of sympathetic nervous system and parasympathetic nervous system. Sympathetic nervous system innervates all organs and tissues including skeletal muscles and CNS. Parasympathetic nervous system innervates heart, esophagus, bronchi, ling,

alveoli, stomach, small intestine, upper large intestine, adrenal gland, kidneys, liver, spleen, genital organs and bladder. Usually the two systems of Autonomic nervous system are in state of dynamic equilibrium. The autonomic functions are regulated through reticular formation and its constituents along with cranial nerve nuclei. The preganglionic fibers of both sympathetic and parasympathetic nervous system as well as postganglionic fibers of parasympathetic nervous system release the neurotransmitter, Acetylcholine (Ach) while postganglionic fibers of sympathetic nervous system release nor-adrenaline and adrenaline as neurotransmitters.

Smoking is one of the most ancient and widespread man's activities. In the early part of 16<sup>th</sup>

century soon after introduction of tobacco into Spain and England by explodes returning for New World, controversy developed from differing opinion as to effects of human use of leaf and products derived from it by combustion or other means. Pipe smoking, chewing and sniffing of tobacco were praised for pleasurable and reputed medicinal actions. At the same time, smoking was considered as foul smelling, loathsome customs, harmful to brain and lungs. Parallel with increasing smoking of cigarettes the controversy has become more and more intense. Scientific attacks upon the problems have increased proportionately. The design, scope and penetration of studies have improved and yield of significant results has been abundant.

From analytical and statistical studies it has been firmly concluded that cigarette smoking has various hazards on different systems of human being as given below.

Cigarette smoking is one of the major risk factor for the development of atherosclerosis, coronary heart disease, acute myocardial infraction and sudden cardiac death. Although smoking increases arterial pressure and heart rate acutely, the effects of smoking on sympathetic activity are not well understood. Smoking has been shown to have varied effects on plasma catecholamine levels, some showed an increase and some showed decrease and other revealed no change, thus leaving a gap in understanding the exact correlation of cigarette smoking and several CVS manifestations like increase blood pressure, heart rate and myocardial O<sub>2</sub> consumption. The present study is chosen to find out the answers to several queries regarding the consequence of smoking on ANS functions with the following aims and objectives. To determine sympathetic and parasympathetic activity in cigarette smokers and compare it with healthy age matched controls in order to find out what influence does smoking have on baroreceptor sympathetic and parasympathetic control mechanisms and to find out for any co-relation between duration of cigarette smoking and autonomic dysfunction.

## 2. Materials and Methods

The present work has been carried out in fifty cigarette smokers and fifty normal, healthy, nonsmokers who served as age matched controls to study autonomic functions as given below in Table No. 1.

**Table No.1: grouping of Subjects**

| Sl. No. | Group                                 | No. of Cases |
|---------|---------------------------------------|--------------|
| 1       | Non Smokers (Normal control subjects) | 50           |
| 2       | Smokers                               | 50           |
|         | A) Smoking in between 5-10 years      | 35           |
|         | B) Smoking more than 10 years         | 15           |

The study is done after obtaining Institutional Ethical Clearance from the Institutional Ethical Committee of Viswabharathi Medical College, Kurnool. The subjects were chosen from general population in and around Kurnool during a period of one year. A careful history was taken regarding Hypertension, Diabetes Mellitus, Asthma, and Giddiness on standing, Syncopal Spell, Visual disturbances, Nocturnal diarrhea, Alcohol consumption and Tobacco chewing. Those with history of the above were excluded from the study in order to rule out from any autonomic involvement. History related to cigarette smoking was taken in detail in regard to number of cigarettes smoked per day, duration of smoking in years and whether full length of cigarette got smoked or not. Autonomic functions involving both sympathetic and parasympathetic were tested by recording blood pressure and heart rate. Blood pressure was measured by Sphygmomanometer as an index of function for sympathetic nervous system function.

Heart rate was determined by using Polyrite recording machine (MEDICARE INCO) as it served as an index for parasympathetic nervous system function. Sympathetic functions were carried out by Cold Pressor Response (CPR) test and Hand Grip test. Parasympathetic functions were tested by Determination of Heart Rate with change in posture (i.e. from Supine to Standing) and Sinus Arrhythmia (change in heart rate with inspiration and expiration). The above tests of autonomic functions were chosen as they were appropriate as described by Bannister [3].

### 2.1 Cold Pressor Test:

Hines & Brown first described this test in 1934 for hypertensive patients [4]. In our study CPR test was carried out in all subjects as per the procedure adopted by Bouchard C [5]. The subject was asked to seat comfortably. Blood pressure on both right and left arm were measured in order to confirm equality on both sides. Then the subject is asked to immerse the left hand in cold water because right hand was used for the other test i.e. Handgrip test in order to avoid undue strain to subject on one hand. The temperature of cold water used for this test was maintained at 4 to 6°C throughout the procedure. Immersion of the hand was 2 inches proximal to wrist crease and the duration being for 2 minutes. Three blood pressure recordings were taken at an interval of 60 seconds.

### 2.2 Handgrip Test:

It provides a form of stress by stimulating sympathoadrenal system. The handgrip test was carried out by using hand grip dynamometer (INCO) which is based on the principle of a simple physical relationship between force and pressure viz  $\text{Force}/\text{Area}=\text{Pressure}^2$ . If area is constant pressure

is directly proportional to force which is expressed in kilogram (Kg). This instrument can provide maximum isometric tension, which serves as an important parameter for physical performance. The subject was asked to seat and relax, he was asked to hold the handgrip with right hand at a constant weight of 15 Kg for 90 seconds throughout the study procedure. The highest of the three readings is taken as the final reading and noted.

**2.3 Parasympathetic System:**

Resting heart rate was measured to test parasympathetic functions by using Polyrite recording machine (Recorder & Medicare System Chandigarh) with mode “ECG” in Lead-II position. The time marker was adjusted to 10 seconds. For determination of heart rate with change of posture the time marker with adjustment of 10 seconds was used and for various phases of respiration (Sinus arrhythmia) the time interval was adjusted to 1 second for 5 seconds in each cycle. All the tests were performed in a comfortable atmosphere. The room temperature being between 27-30°C.

**2.4 Change in posture:**

The subject was asked to lie down in supine position and was relaxed fully. Then electrodes of ECG mode were applied to respective limbs and his heart rate was recorded in supine position by keeping the ECG recording on lead II. The subject was asked to stand erect from supine position to see change in heart rate. The change in heart rate was marked for

every 10 seconds with the help of time markers, Recording of initial 10 seconds was considered for the test.

**2.5 Sinus Arrhythmia:**

The subject was asked to seat comfortably and relax fully. Then he was instructed to take slow but deep inhalation followed by slow and deep exhalation for 5 seconds each. The change in heart rate was recorded during inspiration and expiration. Duration of each cycle i.e. 5 seconds was marked by time marker adjusting it for 1 second. The inspiration was marked by a special marker adjusting it for 1 second. The inspiration was marked by a special marker. Such six successive inspiration and expiration cycles each were recorded for determination of changes to relate any sinus arrhythmia.

**2.5 Statistical Methods**

Statistical analysis was done using IBM SPSS Statistics 20 package. ‘p’-value of <0.05 is considered as statistically significant and ‘p’-value of <0.005 is considered as statistically highly significant.

**3. Results**

Result of table No. 2 showed increase in BP during cold pressor test in both smokers and non-smokers. Smokers revealed more pronounced rise both in systolic as well as diastolic blood pressure as compared to normal healthy controls. Rise in diastolic blood pressure was found to be more significant than rise in systolic blood pressure.

**Table No.2: SBP and DBP Changes during Cold Pressor Test**

|             | No. of Subjects | Mean SBP (mmHg) |        | Mean ± SD increase | p     | Mean DBP (mmHg) |        | Mean ± SD increase | p      |
|-------------|-----------------|-----------------|--------|--------------------|-------|-----------------|--------|--------------------|--------|
|             |                 | Before          | During |                    |       | Before          | During |                    |        |
| Non-smokers | 50              | 101.84          | 119.52 | 18.68 ± 13.25      | <0.02 | 80.8            | 94.24  | 13.44 ± 5.40       | <0.001 |
| Smokers     | 50              | 102.72          | 127.16 | 24.44 ± 9.59       | <0.02 | 80.36           | 100.56 | 20.2 ± 8.61        | <0.001 |

Results of table 3 showed increase in blood pressure during hand grip test in smokers and non-smokers. Smokers revealed more pronounced rise in both SBP and DBP as compared to nonsmokers.

**Table No.3: SBP and DBP Changes during Hand Grip Test**

|             | No. of Subjects | Mean SBP (mmHg) |        | Mean ± SD increase | p      | Mean DBP (mmHg) |        | Mean ± SD increase | p      |
|-------------|-----------------|-----------------|--------|--------------------|--------|-----------------|--------|--------------------|--------|
|             |                 | Before          | During |                    |        | Before          | During |                    |        |
| Non-smokers | 50              | 101.92          | 118.12 | 17.20 ± 6.17       | <0.001 | 81.06           | 95.16  | 14.1 ± 5.49        | <0.001 |
| Smokers     | 50              | 103.16          | 125.72 | 22.56 ± 6.27       | <0.001 | 80.48           | 100.04 | 19.56 ± 6.74       | <0.001 |

Table 4 showed increased heart rate in initial 10 seconds when there is postural change i.e. lying down to standing. This increase is seen in both the groups. But this change had no statistical significance.

**Table No.4: Change in heart rate between Non-smokers and Smokers**

|             | No. of Subjects | Heart rate                  |                           | Mean Increase ± SD | p    |
|-------------|-----------------|-----------------------------|---------------------------|--------------------|------|
|             |                 | Lying down (Avg. in 10 sec) | Standing (initial 10 sec) |                    |      |
| Non-smokers | 50              | 12.47                       | 15.4                      | 2.92 ± 0.85        | <0.8 |
| Smokers     | 50              | 12.85                       | 15.84                     | 2.98 ± 0.85        | <0.8 |

Table 5 showed an increase in heart rate during inspiration and decrease during expiration (sinus arrhythmia) both in smokers and healthy controls but it was not significant statistically.

**Table No.5: Sinus Arrhythmia**

|             | No. of Samples | Mean Inspiration/Expiration $\pm$ SD | p    |
|-------------|----------------|--------------------------------------|------|
| Non-Smokers | 50             | 1.12 $\pm$ 0.08                      | <0.5 |
| Smokers     | 50             | 1.13 $\pm$ 0.06                      | <0.5 |

Table 6 indicates comparison among smokers as per groups. For systolic and diastolic blood pressure changes during cold pressor test, there was an increase systolic as well as diastolic blood pressure. But increase in systolic blood pressure was only significant statistically.

**Table No.6: SBP and DBP Changes during Cold Pressor Test among smokers**

|         | No. of Subjects | Mean SBP (mmHg) |        | Mean $\pm$ SD increase | p     | Mean DBP (mmHg) |        | Mean $\pm$ SD increase | p     |
|---------|-----------------|-----------------|--------|------------------------|-------|-----------------|--------|------------------------|-------|
|         |                 | Before          | During |                        |       | Before          | During |                        |       |
| Group-A | 35              | 101.08          | 123.77 | 22.96 $\pm$ 3.09       | <0.01 | 78.17           | 97.94  | 19.77 $\pm$ 0.89       | >0.01 |
| Group-B | 15              | 106.53          | 135.06 | 28.53 $\pm$ 2.22       | <0.01 | 84.8            | 108    | 23.0 $\pm$ 4.06        | >0.01 |

(Group-A: smoking cigarettes for 5-10yrs and Group-B: smoking cigarettes for more than 10yrs)

Similar comparison in table 7 among smokers for hand grip test showed an increase in systolic and diastolic blood pressure during test, but systolic being significant statistically.

**Table No.7: SBP and DBP Changes during Hand Grip Test among smokers**

|         | No. of Subjects | Mean SBP (mmHg) |        | Mean $\pm$ SD increase | p     | Mean DBP (mmHg) |        | Mean $\pm$ SD increase | p     |
|---------|-----------------|-----------------|--------|------------------------|-------|-----------------|--------|------------------------|-------|
|         |                 | Before          | During |                        |       | Before          | During |                        |       |
| Group-A | 35              | 101.71          | 122.62 | 20.91 $\pm$ 3.15       | <0.01 | 78.62           | 98.28  | 19.66 $\pm$ 1.57       | >0.01 |
| Group-B | 15              | 106.53          | 132.4  | 25.87 $\pm$ 2.76       | <0.01 | 106.4           | 108    | 21.6 $\pm$ 4.52        | >0.01 |

(Group-A: smoking cigarettes for 5-10yrs and Group-B: smoking cigarettes for more than 10yrs)

#### 4. Discussion

Over the last 30 years, there has been in both animals and man a continued interest in cardiovascular effects of smoking. It is generally agreed that nicotine causes significant increase in heart rate and rise in both systolic and diastolic blood pressure, which is thought to be due to stimulation of sympathetic ganglia.

The present study was carried out in 50 smokers (smoking more than 10 cigarettes i.e. 1 pack/day for atleast 5 years) and 50 healthy age matched non-smokers who served as controls for testing autonomic functions. Blood pressure was measured before and during cold pressor test and also during hand grip test to determine sympathetic activity. In our study, there is increase in blood pressure both systolic and diastolic in non-smokers during cold pressor and hand grip test. The results of cold pressor test are in accordance with J Le Blank et al [6] and that of hand grip test similar to Humpheys & Lind [7] & Philip E Creyer [8]. Further heart rate was recorded in nonsmokers for any change with posture (i.e lying down to standing) showed an increase from

lying down to standing in initial few seconds (10 seconds) which is similar to the results of Ewing *et al* [9]. Heart rate was also measured during phases of respiration (sinus arrhythmia) for testing parasympathetic activity.

The results of the present study revealed a significant rise in blood pressure (systolic and diastolic) in smokers as compared with nonsmokers. This is in accordance with the study conducted by Joseph *et al* [10], Otfried *et al* [11], Guido Grassi [12], Gerhart *et al* [13], Neal *et al* [14]. Joseph *et al* [10] studied effects of smoking upon adrenocortical and sympathomedullary activity in 94 males. According to their study there is no change in pituitary adrenocortical andsympathomedullary activity. But 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 (Cold pressor and Hand grip tests). Also criteria for selection of smoker (one half to one pack/day) are smaller than our study (more than 1 pack/day for at least 5 years). In 1999 Gerhardt *et al* [13] studied effects of smoking on baroreceptors in a smoking

more than 6 years. According to their study smoker showed increased blood pressure than non-smokers. These findings are same as per our results. Guido *et al* [12] in their study to understand mechanism responsible for sympathetic activation by cigarette smoking in human opined the pressor and tachycardiac effects of cigarette smoking are associated with plasma catecholamines suggesting an adrenergic stimulation. In our study also there was an increase in blood pressure in smokers over non-smokers which could be explained due to increased sensitivity of sympathetic nervous system due to nicotine to the stimulating tests. According to the study of Kotam Aki M [15] there is increase in basal diastolic blood pressure of smokers over nonsmokers. Such change was not seen in our study. But after handgrip, showed more increase in diastolic BP in smokers than nonsmokers which is similar to that of our study. The study of comparison with smokers and nicotine gums conducted by Neal *et al* [14] concluded that prominent cardiovascular effects of nicotine was a results of activation of sympathetic nervous system because of which smoking increases heart rate and blood pressure. This explanation is plausible with our study. Further the results of cold pressor test and hand grip test when compared for duration of exposure as per following groups.

Group A – duration of smoking between 5 to 10 years,

Group B – duration of smoking more than 10 years.

The finding of this showed more rise in systolic BP during (cold pressor & hand grip) in Group B than in Group A. which was statistically significant ( $P < 0.01$ ). Though diastolic BP showed rise, it was not significant statistically ( $P > 0.01$ ) (Table Nos. 6&7).

In present study, effect of posture on heart rate showed that there is rise in heart rate in initial few seconds(10 sec) from lying down to standing., in both smokers as well as nonsmokers. Also when heart rate was measured during deep inspiration and deep expiration (sinus arrhythmia) an increase was seen during deep inspiration in smokers and nonsmokers as well which showed no statistical significance (Table No.6).Our Study is in correlation with some of the studies while differs with some of the studies [16-32]. Junichiro *et al* [33] was done to study of effects of smoking on vagal function, revealed that heavy smoking causes long term reduction in vagal cardiac control leading to blunted postural response in autonomic cardiac regulation. But our study revealed no such blunting response indicating that affection of vagal control might be delayed sign of smoking. Thus our observations reveal that after cold pressor and hand grip test there is increase in systolic and diastolic BP in habitual smokers, which is statistically

significant when compared with age matched controls, indicating change in sympathetic activity. But the effects of postural change and respiratory phase on heart rate (sinus arrhythmia) were same in smokers as well as in nonsmokers revealing no affection of parasympathetic system.

Thus we conclude that habitual smoking affects the sympathetic activity earlier than parasympathetic activity. Kai E Laustiola[34] showed that long term smoking induces down regulation of  $\beta$  adrenergic receptors, though plasma catecholamine levels were significantly higher in smokers than nonsmokers as explained by  $\beta$  blockers which were less effective in the treatment of hypertension in smokers as compared to nonsmokers. Their observations indicate that cigarette smoking might induce  $\alpha$  adrenergic tone with considerable impact on cardiovascular regulations. Further these results implied even if  $\alpha$  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 cold pressor and handgrip test the rise in BP was higher in smokers over nonsmokers could 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.

## 5. Conclusion

The present study has been carried out in 50 smokers and 50 nonsmokers (control) to study the effect of habitual smoking an autonomic function, which include cold pressor test and hand grip test for checking sympathetic activity and postural changes in heart rate and sinus arrhythmia for testing parasympathetic activity. The results were compared with age matched controls and the same were analyzed for statistical significance using standard 'P' test. An increase in blood pressure both systolic and diastolic in smokers and nonsmokers was found with cold pressor test and handgrip test. The rise in blood pressure of smokers was more than that of nonsmokers, indicating the increased sensitivity of sympathetic nervous system. There was no significant comparative change in heart rate in smokers and nonsmokers when tested for postural change and for sinus arrhythmia indicating no change in parasympathetic nervous system. There was increase in both systolic and diastolic blood pressure among smokers during cold pressor test and handgrip test. A positive correlation was found when this increase in blood pressure in smokers was compared with duration of smoking in years.

The present study of autonomic functions in cigarette smokers reveals that cigarette smoking affects cardiovascular functions as indicated by rise in BP in smokers than nonsmokers reflects the sensitivity of sympathetic activity to nicotine due to smoking. The duration of exposure of smoking though showed systolic rise, a positive correlation could not be established by the results of present study. Thus the study concludes that smoking possibly has an effect on various parts of neuro-cardiovascular regulation system altering the sensitivity of ANS activity in habitual smokers. Presently, it is difficult to explain the exact mechanism responsible for long term effects of smoking on autonomic functions, prompting further careful planned studies in this regard.

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