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The Effect of Smoking on the Cardiovascular Autonomic Functions: A Cross Sectional Study

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ABSTRACT

Introduction: Smoking is a worldwide major cause of preventable morbidity and mortality. Smoking affects the cardiovascular system by several mechanisms. The present study was planned to study the effect of smoking on the cardiovascular autonomic functions among smokers.

Material and Methods: Hundred male subjects who were in the age group of 25 to 40 years, who included 50 smokers and 50 non – smokers who formed the control group were selected for the present study. The participant subjects were selected from among the staff members, residents and the patients from the routine OPD. Prior informed written consents were obtained from them after explaining to them, the procedure and the purpose of the study tests. The Cardiovascular Autonomic Function Tests were assessed by using a CANWIN AUTONOMIC ANALYSER which was available in the department.

Results and Conclusion: After applying the 'Z'-test for the difference between the two sample means, it was observed that there was a highly significant difference between the mean values of the para-sympathetic function tests among the smokers and the non – smokers (i.e. $p<0.01$) The Resting Heart Rate had significantly increased and the Expiration: Inspiration Ratio, the 30:15 Ratio (Response to standing) and the Valsalva Ratio had significantly decreased in the smokers as compared to those in the non – smokers. After applying the 'Z'-test for the difference between the two sample means, it was observed that there was no significant difference between the mean values of the Postural hypotension test (i.e. $p>0.05$) and that there was a highly significant difference between the mean values of the Sustained handgrip test in the smokers and the non – smokers (i.e. $p<0.01$).

Key words: Cardiovascular autonomic function tests, Smoking, Resting heart rate

INTRODUCTION

Smoking is a worldwide major cause of preventable morbidity and mortality [1]. About 17% smokers in the world live in India [2]. Presently, nearly 2200 people per day and 9 lacs every year die in India due to tobacco related diseases. The Health Ministry has estimated that 40% of India's health problems stem from tobacco use [3]. The health and lifestyle factors, together with the genetic makeup of an individual, determine the response to these changes [4]. Heavy smoking is the commonest cause of ischaemic heart disease and death in the 30 – 40 years of age group, who are likely to be free from other myocardial risk factors [5].

Smoking affects the cardiovascular system by several mechanisms. The haemodynamic effects of smoking appear to be mediated by nicotine. Such effects cause an increase in the myocardial work. Nicotine increases the cardiac output by increasing both the heart rate and the myocardial contractility [1]. The autonomic alterations may contribute to the increased cardiovascular risk which is present in smokers. The pressor and the tachycardial effects of cigarette smoking are associated with an increase in the plasma catecholamines, thus suggesting that these effects are dependent on the adrenergic stimulation. Smoking is accompanied by a marked and a prolonged increase in the heart rate and the blood pressure [6]. Smoking impairs the baroreflex sensitivity in humans, which may contribute to the smoking induced increase in the blood pressure and the heart rate, as well as to the concomitant alterations in their variability [7]. The autonomic neurohumoral response which is evoked by smoking, results in the down regulation of the beta-adrenergic receptors in long term smokers [8].

In recent years , the study on the cardiac autonomic modulation in human subjects has been greatly facilitated by the development of computer based methods for the spectral analysis of the heart rate variability and the spontaneous baroreflex function [9 – 11]. With this background in mind, it was decided to study the correlation between smoking and the cardiovascular autonomic functions among smokers and non – smokers.

MATERIAL AND METHODS

The present cross sectional study was carried out in the Department of Physiology, Rural Medical College, Pravara Institute of Medical Sciences, Loni, India, during August 2009 to July 2011 and it was approved by the Institutional Ethical and Research Committee.

Hundred male subjects who were in the age group 25 to 40 years, who included 50 smokers and 50 non – smokers who formed the control group were selected for the present study. The participant subjects were from among the staff members, residents and the patients from the routine OPD. Prior informed written consents were obtained from them after explaining to them, the procedure and the purpose of the study tests.

Inclusion and Exclusion Criteria

The Case Group: Smokers with a history of smoking of more than 5 years were considered as the case group for the present study. Those with a history of smoking of less than 5 years were excluded from the present study. Also, the subjects with a history of any major illness like Hypertension, Diabetes Mellitus, and Peripheral

Neuropathy in the past or present were also excluded from the present study.

The Control Group: The subjects who had never smoked in life and who did not have any other addiction which was related to tobacco were considered as the control group for the present study. The subjects with any form of addiction and also with a history of any major illness like Hypertension, Diabetes Mellitus, and Peripheral Neuropathy in the past or present were excluded from the present study.

The Smoking Index [12]: This is a parameter which is used to express the smoking exposure quantitatively. This is especially useful in defining the risk ratio of a smoking related disease. Here, the smoking index was calculated by multiplying the average number of cigarettes which was smoked per day and the duration of the smoking in years. The number of cigarettes meant, the average numbers of cigarettes which was smoked per day in the past seven days.

According to the Smoking Index, the smokers were classified into:

1. Light smokers (Smoking index 1-100)
2. Moderate smokers (Smoking index 101-200)
3. Heavy smokers (Smoking index >201)

The Cardiovascular Autonomic Function Tests were assessed by using a CANWIN AUTONOMIC ANALYSER which was available in the department. CANWIN is a state of the art, PC window based Cardiac Autonomic Neuropathy analysis system which is manufactured by Genesis Medical System Pvt. Ltd, Hyderabad, India. It has an extensive data base to keep track of the subjects' history and for archive test retrieval and comparisons. Being fully automatic, the need of a manual recording and reading is eliminated. An inbuilt time domain waveform analysis and blood pressure measurements make the task of conducting all the six autonomic functions tests very easy.

The following cardiovascular autonomic function tests were included:

Parasympathetic Function Tests

1. **The Resting Heart Rate:** The subjects were asked to lie comfortably for 15 minutes. The ECG was recorded continuously for 1 minute. The resting heart rate was calculated from the ECG.
2. **The Expiration–Inspiration Ratio (E: I Ratio):** The subjects were asked to take deep inspirations for 5 seconds, followed by deep expirations for 5 seconds. The ECG was recorded for 3 such cycles. This test is based on the sinus arrhythmia during each respiratory cycle, which depends on the variation in the vagal tone.
3. **The 30:15 Ratio:** (Response to standing) The subjects were asked to lie down comfortably over the couch and then they were asked to stand up. Their heart rates were recorded at the 15th and 30th beats immediately after standing.
4. **The Valsalva Ratio:** The subjects were asked to sit comfortably. Their heart rates were recorded at rest, with the ECG. Their noses were clipped with nose clips and mouth pieces were inserted between their teeth and lips. The other ends of the mouthpieces were connected to mercury manometers. The subjects were asked to blow air into the mouthpieces and the pressure was maintained at 40 mmHg for 15 seconds. The ECG was continuously recorded.

The valsalva ratio was calculated as the ratio of the longest RR interval after the strain to the shortest RR interval during the strain.

Sympathetic Function Tests

1. **The Postural Hypotension Test (Postural challenge test):** The subjects were asked to lie comfortably in the supine position for 15 minutes and their blood pressures were recorded. They were then asked to stand up and their blood pressures were recorded immediately and after 1 minute.
2. **The Sustained Handgrip Test:** The subjects were asked to hold spring dynamometers in their left hands and to compress them maximally and the values were noted. Then they were asked to hold the spring dynamometers in their left hands and to compress them to upto 30% of the maximum and to hold them for 4 minutes. The rise in the diastolic blood pressure at the point, just before the release of the handgrip, was noted. This test is an indicator of the sympathetic insufficiency.

The collected data was analyzed by using the SPSS software which was available in the department.

Observations and Results

After applying the 'Z' test for the difference between the two sample means, a highly significant difference was observed between the mean values of the **Para sympathetic function tests** in the smokers and the non – smokers (i.e. p<0.01) It was seen that the Resting Heart Rate had significantly increased and that the Expiration: Inspiration Ratio, the 30:15 Ratio (Response to standing) and the Valsalva Ratio had significantly decreased in the smokers as compared to those in the non – smokers [Table/Fig-1].

After applying the 'Z' test for the difference between the two sample means, no significant difference was observed between the mean values of the Postural hypotension test (i.e. p>0.05) and a highly significant difference was observed between the mean values of the Sustained handgrip test in the smokers and the non – smokers (i.e. p<0.01) [Table/Fig-2].

In [Table/Fig-3], it can be seen that as far as the para sympathetic function tests were concerned, the values of (1) the Expiration: Inspiration ratio, (2) the 30:15 ratio and (3) the Valsalva ratio went on decreasing as the severity of the smoking (smoking index) increased, thus indicating a greater damage to the parasympathetic system. Also, the resting heart rate values went on increasing with the severity of smoking, thus suggesting a similar effect.

	Smokers (n=50)	Non – smokers (n=50)			
Para sympathetic function tests	Mean ± SD	Mean ± SD	Z test value	'p' value	Significance
Resting Heart Rate (/min)	78.36 ± 5.55	70.54 ± 4.68	7.62	p<0.01	HS
Expiration: Inspiration Ratio	1.16 ± 0.14	1.39 ± 0.16	7.66	p<0.01	HS
30:15 Ratio (Response to standing)	0.99 ± 0.12	1.09 ± 0.13	4.0	p<0.01	HS
Valsalva Ratio	2.87 ± 1.09	4.89 ± 1.24	8.66	p<0.01	HS

[Table/Fig-1]: Comparison of mean values of autonomic function tests in smokers and non – smokers (Para-sympathetic function tests)
HS = Highly significant

Sympathetic function Tests	Smokers (n=50)	Non-smokers (n=50)	Z test value	'p' value	Significance
	Mean ± SD	Mean ± SD			
Postural Hypotension Test (Fall in systolic Pressure) (mmHg)	8.04±3.46	8.20±4.21	0.21	p>0.05	NS
Sustained handgrip Test (Rise in diastolic Pressure) (mmHg)	6.12±2.8	9.06±3.64	4.53	p<0.01	HS

[Table/Fig-2]: Comparison of mean values of autonomic function tests in smokers and non – smokers: (Sympathetic function tests)
NS = Not Significant and HS = Highly Significant

Smoking Index	Resting Heart Rate (/min)	E : I Ratio	30:15 Ratio	Valsalva Ratio
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
1-100 (Light smokers) (n=31)	77.29 ± 6.31	1.22 ± 0.09	1.03 ± 0.12	3.66±2.78
101- 200 (Moderate smokers) (n=11)	79.36 ± 2.80	1.08 ± 0.12	0.90 ± 0.06	3.14±2.67
Above 200 (Heavy smokers) (n=8)	81.12 ± 4.26	1.04 ± 0.19	0.93 ± 0.06	1.81±2.47

[Table/Fig-3]: Correlation of Smoking index and Para-sympathetic function tests in Smokers

Smoking Index	Postural Hypotension Test	Sustained Handgrip Test
	Mean ± SD	Mean ± SD
1-100 (Light smokers) (n=31)	7.84 ± 3.49	6.16 ± 3.0
101-200 (Moderate smokers) (n=11)	7.36 ± 3.70	6.18 ± 2.67
Above 200 (Heavy smokers) (n=8)	9.75 ± 2.76	5.87 ± 2.47

[Table/Fig-4]: Correlation of Smoking index and Sympathetic function tests in smokers:

In [Table/Fig-4], it can be seen that in the postural hypotension test, the fall in the systolic pressure was maximum in the heavy smokers as compared to those in the light and the moderate smokers. Similarly, in the sustained handgrip test, the rise in the diastolic pressure decreased in the heavy smokers as compared to those in the moderate and the light smokers.

DISCUSSION

Coronary Artery Disease (CAD) is a major cause of premature death and disability throughout the world. Tobacco use is an important and an avertable cause of CAD. The use of tobacco is on the rise worldwide, especially among the youth [13].

The sympathetic activation which is induced by smoking, depends on an increased release and/or a reduced clearance of the catecholamines. The central sympathetic activity is inhibited by smoking, presumably via a baroreceptor stimulation which is triggered by the smoking-related pressor response. The baroreflex is impaired by smoking and a partial inability in reflexly counteracting the effect of the sympathetic activation is also responsible for the pressor response. The haemodynamic changes are associated with a marked and a prolonged increase in the plasma norepinephrine and the epinephrine levels, which has prompted the hypothesis that the mechanisms which are responsible for the pressor and the tachycardic responses have an adrenergic nature [14]. In the present study, after the statistical analysis, it was seen that significant changes were found in the parasympathetic and to some extent, in the sympathetic autonomic function tests in the smokers as compared to those in the non – smokers.

In the present study, the resting heart rate was found to be statistically highly significant in the smokers (78.33 ± 5.55/min) as compared to that in the non – smokers (70.54 ± 4.68/min). The resting heart rate is considered to be a good barometer of the overall cardiac health and it is mainly governed by the para-sympathetic activity. The resting heart rate is a simple measurement with prognostic implications. The high resting heart rate is a predictor of the total and the cardiovascular mortalities which are independent of other risk factors in the patients with coronary artery disease [15]. Some studies pointed out that an elevated heart rate was a risk marker of the cardiovascular diseases which were common in the general population and that it placed a high burden of disability and mortality [16].

The 30:15 ratio or the response to standing is a parameter which is useful for assessing the reactivity of the para-sympathetic system. In the present study, a decrease in the 30:15 ratio was found to be statistically highly significant in the smokers (0.99 ± 0.12) as compared to that in the non – smokers (1.09 ± 0.13), thereby indicating a reduced para-sympathetic activity. The expiration: inspiration ratio is based on the sinus arrhythmia during each respiratory cycle, which depends on the variation in the vagal tone. In the present study, a highly significant decrease in the expiration: inspiration ratio was observed in the smokers (1.16 ± 0.14) as compared to that in the non – smokers (1.39 ± 0.16). G.A.Gould et al., (1986) also found statistically highly significant changes in the 30:15 ratio and the Expiration: inspiration ratio in smokers as compared to those in the non – smokers [17].

The valsalva ratio is another reliable indicator of the parasympathetic activity, which is responsible for the recovery of the heart rate after strenuous activities like the Valsalva maneouvre. The manoeuvre creates a high intra-thoracic pressure which evokes a complex circulatory response with four phases. Our study showed that smokers (4.89 ± 1.24) had a lower value of the Valsalva ratio as compared to the non – smokers (2.87 ± 1.09), thus indicating a derangement of the parasympathetic function. Other research workers, Mervi et al., [18] and Beatriz et al., [19] also found similar results.

In the postural hypotension test, we measured the changes in the degree of the postural hypotension by recording the fall in the systolic blood pressure as an index of the sympathetic activity and we observed that there were no significant changes in the smokers (8.04 ± 3.46) as compared to those in the non – smokers (8.20

± 4.21). This was apparently due to the more numbers of light smokers (n = 32) as compared to heavy smokers (n = 8) in this study. It could be possible that in some of these cases, an early involvement of the sympathetic system may be present, which may have not been evident or overt. At the same time, it may be pointed out that the fall in the systolic pressure was greater in the heavy smokers as compared to that in the light smokers, though it was not statistically significant. However, in other studies, significant changes were seen in the postural hypotension test.

In the sustained handgrip test, we measured the rise in the diastolic blood pressure at the point, just before the release of the handgrip. In the present study, it was seen that the rise in the diastolic pressure was significantly less in the smokers (6.12 ± 2.8) as compared to that in the non – smokers (9.06 ± 3.64), thus suggesting a decrease in the sympathetic reactivity. Mervi et al., (1994) also found that the rise in the diastolic pressure was significantly less in the smokers as compared to that in the non – smokers, thus suggesting a decrease in the sympathetic reactivity [18].

LIMITATIONS OF THE PRESENT STUDY

In the present study, we compared the autonomic function test parameters between the smokers and the non – smokers and we tried to assess the severity of the autonomic alterations on the basis of the smoking index parameter. However, we did not measure the plasma nicotine or the epinephrine levels and we also did not correlate them with the autonomic changes. Also, in this study, the baseline activities of the para-sympathetic and the sympathetic systems were studied, excluding the acute effects of smoking.

CLINICAL APPLICATIONS

The cardiovascular autonomic function tests are reliable, non-invasive and easy to carry out. By using these simple tests, we can detect the early involvement of the autonomic nervous system before the clinically related symptoms appear and they are thus useful in taking steps to prevent the further progress of the disease.

REFERENCES

[1] Satyavan Sharma. New approaches in smoking Cessation. *Indian Heart Journal*, March-April 2008; 60 (2): B-34-37.
[2] John R, et al. Tobacco consumption patterns and it's health implications in India. *Health policy*. Feb. 2005;71;213-22.
[3] Newspaper report: The Times of India, Health for the millions, New Dehli, 11 March 2010.
[4] Shiveta Bansal, Aman Bansal. Effect of Age and Sex on the R-R interval in ECG of Healthy Individuals. *Indian Journal of Basic and Applied Medical Research*; June 2012; 1(3): 178-84
[5] Mrunal Shenwai, NV Aundhakar. Effect of cigarette smoking on various haematological parameters in young male smokers. *Indian Journal of Basic and Applied Medical Research*; December 2012; 2(5): 386-92.
[6] G Grassi, Mechanisms responsible for sympathetic activation by cigarette smoking in humans, *Circulation*,1994;90;248-53.
[7] G Manecia, Smoking impairs baroreflex sensitivity in humans, *Circulation*: 1997; 273 (3): 1555-60.
[8] KL Laustiola, et al. A study of monozygotic twin pairs discordant for smoking. *American heart association journal*: 1988; 78;1234-40.
[9] Akselroad, et al. Power spectral analysis of the heart rate fluctuation: a quantitative probe of beat to beat cardiovascular control. *Science*. 1985;213: 220-21.
[10] Akselroad, et al. Haemodynamic regulation: investigation by spectral analysis. *American Journal of Physiology*. 1985; 249: H-867-75.
[11] B Erger, et al. Transfer function analysis of autonomic regulation. *American Journal of Physiology*. 1989;256: H-142-52.
[12] SK Gupta. Respiratory disorders among workers in a railway workshop. *Ind. Journal of Tuberculosis*.1995;42:161.
[13] Prathamesh H Kamble, Mamta V Rode, Mrunal S Phatak, Prashant Tayade. Is Smokeless Tobacco using a risk factor for Coronary artery disease? A comparative study of smokers and smokeless tobacco users. *Indian Journal of Basic and Applied Medical Research*. December 2011: 1(1): 22-30.
[14] Ambrose JA, Barua RS. The pathophysiology of cigarette smoking and cardiovascular disease: An update. *Journal of American College of Cardiology*, 2003. PIMD:15145091.
[15] Health effects of Tobacco. www.wikipedia.org/wiki/effects of tobacco.
[16] Ariel Diaz, Martial G. Bourassa1, Marie-Claude Guertin, Jean-Claude Tardif 1 Long-term prognostic value of resting heart rate in patients with suspected or proven coronary artery disease. *European Heart Journal*: 2005; 26(10): 967-74.
[17] GA Gould, M Ashworth, GT Lewis. Are cardiovascular reflexes more commonly impaired in patients with bronchial carcinoma? *Thorax,* 1986;41:372-75.
[18] Mervi Kotamäki. Smoking induced differences in autonomic responses in military pilot candidates, *Clinical Autonomic Research*, 5(1): 31-36.
[19] Beatriz Martins Manzano, Luiz Carlos Marques Vanderlei, Ercy Mara Ramos, Dionei Ramos. Acute effects of smoking on autonomic modulation. *Arq Bras Cardioly*. 2011 Feb;96(2):154-60.

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