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Research Article

EFFECT OF SMOKING ON HEART RATE VARIABILITY IN NORMAL HEALTHY VOLUNTEERS

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ABSTRACT

Objective: The aim of this study is to determine the effect of tobacco smoke on heart rate variability (HRV).

Methods: This study included 90 male smokers (30-mild, 30-moderate, 30-severe) (Group II) and 30 age-matched non-smokers as controls (Group I). HRV analysis was performed using 8 channels Physiopac of Medicaid Company. All the subjects were subjected to HRV test. The short-term 8 minutes HR recording was performed for HRV analysis.

Results: Mean RR, mean HR, root mean square of the successive differences, of the smokers and non-smokers, did not differ significantly. However, smokers NN50, Pnn50, high frequency (HF) declined significantly, and the smokers show significantly higher low frequency (LF), LF/HF ratio when compared with those of the non-smoking individuals ($p<0.05$).

Conclusion: HRV analysis of smokers and nonsmokers showed that smoking subjects had an autonomic imbalance suggestive of an increased sympathetic tone or decreased parasympathetic tone. Sympathetic overactivity may lead to cardiovascular disease development in smokers.

Keywords: Smoking, Healthy volunteers, Heart rate variability.

INTRODUCTION

In India, smoking is a common habit particularly in young adults for psychosocial reasons then it becomes a regular habit because of pharmacological properties of nicotine, it plays a major part in persistence, conferring some advantages to the smoker's mood. Very few cigarette smokers (<2%) can limit themselves to occasional or intermittent smoking. Various forms of tobacco smoking are practiced here, including cigarettes, Beedis, chillum (clay pipe), chutta (reverse smoking), and hukku (hubble-bubble) are also available [1]. The first two are being the predominant types in urban areas. They contain tobacco and harmful chemicals which is injurious to our health.

The World Health Organization reported that tobacco smoking killed 100 million people worldwide in the 20th century and warned that it could kill one billion people around the world in the 21st century. By early 2030, tobacco-related death would increase to about 10 million a year [2].

Tobacco smoke contains more than 4000 chemicals and around 40 carcinogens, including nicotine, tar, carbon monoxide (CO), methoprene, propylene glycol, benzopyrene, butane, cadmium, acetone, ammonia, lead, benzene, and formaldehyde [3].

Statistically, each cigarette smoked, shortens the user's life by 11 minutes. About half of cigarette smokers die of tobacco-related disease and lose on average 14 years of life. Cigarette use by pregnant women has also been shown to cause birth defects, including mental and physical disabilities [4].

Smoking has both short- and long-term effects on the body. Smoking just one cigarette can have immediate health effects [5], including: Temporary increases in blood pressure and heart rate (HR); Constriction of blood vessels, which slows down blood flow around the body; and binding of CO to hemoglobin in the bloodstream. This reduces the amount of oxygen delivered to the tissues.

Cigarette smoking is a strong risk factor for acute ischemic cardiac events such as myocardial infarction and sudden death, but it is much less a risk factor for chronic ischemic syndromes such as angina pectoris [5]. Smoking makes the heart work much harder, reduces its oxygen supply, makes clots more likely to form in blood vessels, and increases the risk of potentially fatal changes in the heart beat [6].

Both mainstream (directly inhaled) tobacco smoke and sidestream (environmental or passively inhaled) tobacco smoke have been shown to negatively affect cardiovascular health [6]. Overall, smokers have a 70% greater risk of death from coronary heart disease than non-smokers [7]. Even smoking 1-4 cigarettes/day can double or triple the risk of coronary disease [6,8]. The risk increases with the number of years of smoking and number of cigarettes smoked [6,9].

HR variability (HRV) is the degree of fluctuation in the length of the intervals between heart beats [10]. HRV is mirroring the regularity of heart beats: Bigger regularity - lowers HRV (and *viz.*). Regularity of heartbeats is derived from a quantity of numbers; equal to the times elapsed between successive heartbeats. They are named RR intervals and are measured in a millisecond. RR intervals are obtained from electrocardiogram (ECG). Hence, this study proposed to determine the effect of smoking on the HRV in normal healthy volunteers.

METHODS

This prospective study was carried out in the research laboratory of the Department of Physiology of SRM Medical College and Research Centre. This study included 90 (30-mild, 30-moderate, 30-severe) male smokers (Group II) and 30 age-matched healthy males as controls (Group I). The study was approved by the institutional ethical committee and a written consent form was obtained after the explanation of the procedure before initiation of the study.

The study included male subjects of age between 20 and 40 years, 90 smokers (30-mild, 30-moderate, 30-severe) and 30 non-smokers. Participants were excluded if they were known to have cardiac

disease, history of alcohol abuse. Those under medication that affects HR, hypertension, diabetes mellitus, sleep apnea, chronic obstructive pulmonary disease, renal failure, depression, and obesity.

Following which study was initiated. A thorough history was collected from all the participants including personal details such as name, age, sex, address and phone number, smoking history, medical history including history of any respiratory and cardiac disease. Height, weight, Body mass index (BMI), and blood pressure were recorded for all subjects. BMI was calculated using the following formula:

BMI = Weight in kg/(height in m)^2

HRV analysis

All the subjects were subjected to HRV test. The short-term 8 minutes HRV recording was performed for HRV analysis using 8 Channel Physiopac of Medicaid Company.

- The subject was asked to lie down comfortably in the supine position in the laboratory
- The ECG electrodes were placed on the limbs of the subject and were connected to the leads of the machine for lead II ECG recording. The ECG was recorded for 8 minutes
- HRV analysis was performed using the HRV analysis software version 1.1.

Technical aspects

HRV can be quantified in the time and frequency domains, the time-domain measures include the usual tool of assessment of variation, as is performed in statistics. The time domain is easier to assess, but finer aspect of variations are not appreciated. In a short period, the overall magnitude of HRV is assessed well, but the individual contribution of various factors is not elucidated. Variations in instantaneous HR can be assessed spectrally.

RR tachogram is plotted using the RR intervals in the 8 minutes lead II ECG. The RR tachogram is considered as a non-periodic signal which transformed to its frequency spectrum using the fast Fourier transform algorithm or autoregressive modeling. The biggest advantage of this complex mathematical variation in different frequency band corresponds to the activity of different physiological systems.

HRV components

The power spectrum of HRV in mammals usually reveals three spectral components

- A high-frequency band (HF) 0.15-0.4 hz
- A low-frequency band (LF) 0.04-0.15 hz
- A very LF band (VLF) 0.0-0.04 hz.

HF

The HF component is caused by Vagal tone, during the respiratory cycle. The inspiratory inhibition of Vagal activity is evoked centrally in the cardiovascular center. In addition, peripheral reflexes arising from the thoracic stretch receptors contribute to this so-called respiratory sinus arrhythmia (RSA). RSA is clearly abolished by atropine or Vagotomy and the power of the HF component is used as an index of Vagal modulation.

LF

The LF component of HRV is characterized by an oscillatory pattern, with a period of 10 seconds. This rhythm originates from self-oscillation in the vasomotor part of the baroreflex loop as a result of negative feedback, and it is commonly associated with synchronous fluctuations in blood pressure, the so-called Mayer waves.

VLF

The VLF component account for all other HR changes include those associated with thermoregulation and hormonal and local factors.

HRV indices

HRV analysis has two components: Time domain and frequency domain. The HRV assessed by calculating indices is based on a statistical operation on RR intervals (time-domain analysis) or by spectral analysis of an array of RR interval (frequency-domain analysis).

Both methods require accurate timing of R-waves. The analysis performed on 8 minutes ECG recording is called short-term HRV and HRV of the 24 hrs ECG recording is called long-term HRV.

Time-domain analysis

Two types of HRV indices are distinguished in the time-domain analysis. Beat to beat or short-term variability indices represent fast changes in HR. Long-term variability (LTV) indices are slower fluctuations. Both types of indices are calculated from the RR intervals occurring in chosen time window.

RESULTS

The Participants characteristic are presented in Figure 1 for both the groups. Age, height, weight, and BMI were taken for all participants; both the groups were not significantly different from each other as the p>0.05.

Table 1 compares the time domain parameters of HRV between Group I (non-smokers) and Group II (smokers). For RR, the mean±standard deviation in Group I (non-smokers) was 0.69±0.21 and Group II (smokers) was 0.74±0.18. The p=0.232 is not significant.

The mean ± standard deviation for HR in Group I (non-smokers) was 74.21±6.88 and Group II (smokers) was 75.82±7.45. The p=0.299 which is not significant.

The mean±standard deviation of RMSSD in Group I (non-smokers) was 26.13±11.6 and Group II (smokers) was 22.53±11.49.

Mean±standard deviation of NN50 in Group I (non-smokers) was 24.53±6.21 and in Group II (smokers) was 20.91±7.56. The p=0.020 which is significant.

The mean±standard deviation of Pnn50 in Group I (non-smokers) was 5.17±2.99 and in Group II (smokers) was 3.74±2.50. The p=0.011 which is significant.

The difference in NN50 between smokers and non-smokers and was categorized into 3 different Groups – Control (non-smokers) and mild, moderate, severe (severity of smokers). Shown in Figure 2.

Figure 3 Compares the difference in Pnn50 between Control (non-smokers) and mild, moderate, severe (severity of smokers).

Comparison of the RMSSD between control (non-smokers) and mild, moderate, severe (severity of smokers) are shown in figure 4, The

Table 1: Comparison of time domain data between smoking and control group

Parameter	Mean±SD		p value
	Group I Control (n=30)	Group II Subject (n=90)	
Mean RR	0.69±0.21	0.74±0.18	0.232
Mean HR	74.21±6.88	75.82±7.45	0.299
RMSSD	26.13±11.6	22.53±11.49	0.141
NN50	24.53±6.21	20.91±7.56	0.020
Pnn50	5.17±2.99	3.74±2.50	0.011

HR: Heart rate, RMSSD: Root mean square of the successive differences, SD: Standard deviation

p value of mild and moderate smokers was <0.05 which is not significant and for severe: 0.000 which is highly significant.

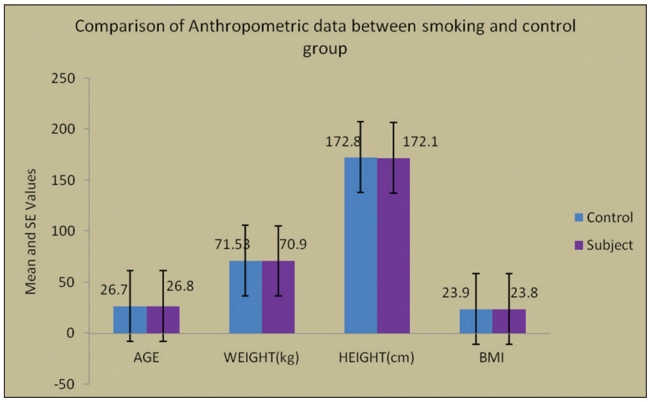

Fig. 1: Comparison of anthropometric data between smoking and control group

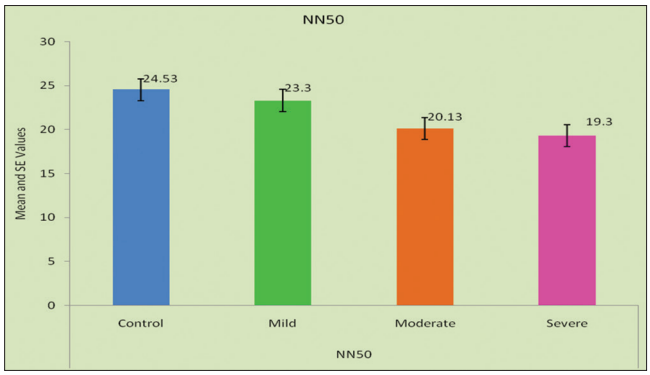

Fig. 2: Compares the NN50 between smokers and control group

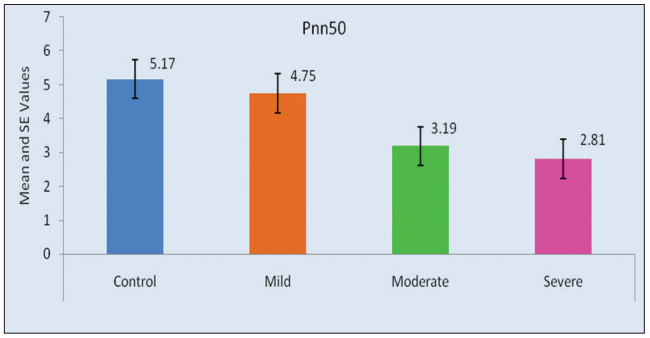

Fig. 3: Compares the Pnn50 between smokers and control group

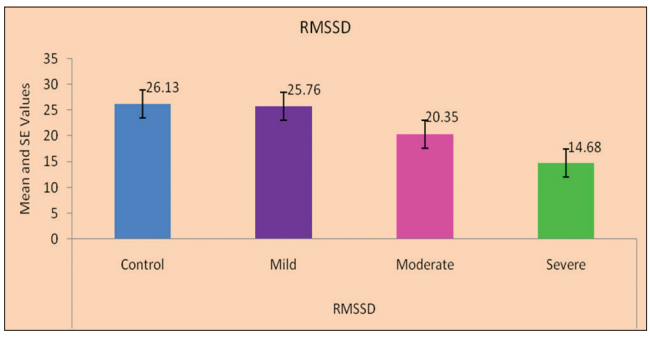

Fig. 4: Compares the root mean square of the successive differences between smokers and control group

Comparison of dependent variables, mean difference in respiratory rate between control group, mild, moderate and severe smokers are shown in Table 2. Mean difference and standard error in Heart rate between all the groups are shown in Table 3.

Comparison of high frequency (FFT – Non parametric spectrum power ms^2) between the groups are shown in Figure 5, mean difference in low frequency domain (FFT – Non parametric spectrum power ms^2) between control, mild, moderate and severe are shown in figure 7.

Figure 6 shows the comparison between LF/HF between smoking and control group. Table 4 shows the mean difference between the groups; and significant changes in p value which is 0.000.

DISCUSSION

The autonomic nervous system and the balance between parasympathetic and sympathetic output play an important role in overall cardiovascular homeostasis. Hence, we planned to find the effect of smoking on a cardiac autonomic function by analyzing the HRV.

In this study, we included both smokers and non-smokers, Fig. 1 shows similar characteristic variables of age, height, weight, BMI between the Groups I and II. Analysis of time domain HRV parameters NN50 and Pnn50 were significantly reduced in smokers compared to non-smokers which are explained in Table 1 and Figs. 2 and 3. However, there was no significant difference in mean HR, mean RR, and root mean square of the successive differences (RMSSD) between the two groups.

In this study, it was observed that mean RR was comparatively higher in smokers than control group individuals, especially much higher mean RR was found in severe smokers (Table 2). When mean HR was compared between the groups, it was found that control group and smokers both had similar mean value, and severe smokers had higher HR compared

Table 2: Compares the mean RR between smokers and control group

Dependent variable	Group	Mean	Standard error	Significant
Mean RR	Control	0.69	0.03	
	Mild	0.71	0.50	0.984
	Moderate	0.75	0.50	0.712
	Severe	0.77	0.50	0.435

Table 3: Compares the mean HR between smokers and control group

Dependent variable	Group	Mean	Standard error	Significant
Mean HR	Control	74.21	1.25	
	Mild	74.36	1.86	1.000
	Moderate	74.87	1.86	0.985
	Severe	78.23	1.86	0.143

HR: Heart rate

Table 4: Comparison of frequency domain data between control group and smokers

Parameter	Mean±SD		p value
	Group I Control (n=30)	Group II Subject (n=90)	
LF	57.55±2.16	60.50±2.98	0.000
HF	30.13±1.89	27.06±2.49	0.000
LF/HF	1.912±0.07	2.258±0.25	0.000

LF: Low frequency, HF: High frequency, SD: Standard deviation

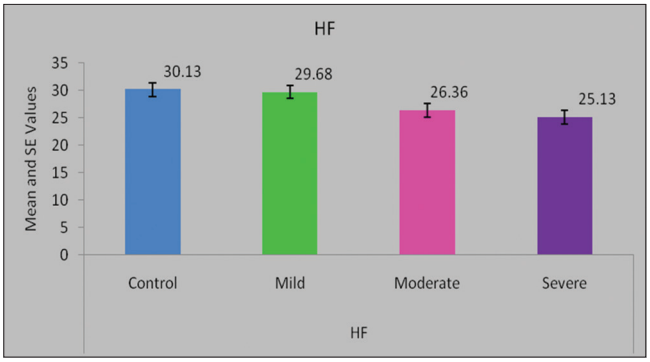

Fig. 5: Compares the high frequency between smokers and control group

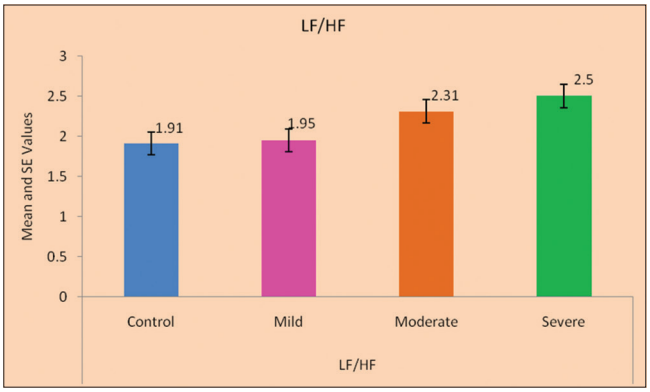

Fig. 6: Compares the low frequency/high frequency between smoking and control group

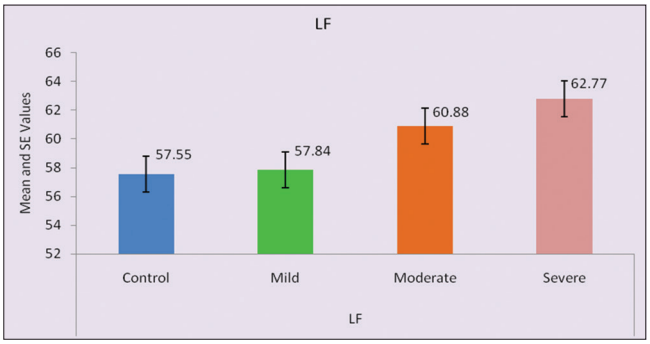

Fig. 7: Compares the low frequency between smokers and control group

with mild and moderate smokers shown in Table 3. According to Karakaya *et al*. acute cigarette smoking alters HRV parameters. The mean RR interval, the standard deviation of RR interval, and the root mean square of successive RR interval differences were significantly decreased [11]. Fig. 4 shows the mean differences between the groups for RMSSD which is significantly reduced in smokers compared to control group. Acute smokers known to have mild changes compared to severe smokers.

Barutcu *et al*. investigated cardiac autonomic function in heavy smokers and non-smokers by analysis of HRV. 24 long-term heavy smokers (men) and 22 non-smoker subjects were included in the study. Time domain (mean RR interval, the standard deviation of RR interval index (SDNN), and the RMSSD) and frequency domain (HF, LF, and LF/HF ratio) parameters of HRV were obtained. They concluded that vagal modulation of the heart was blunted in heavy smokers, particularly during a parasympathetic maneuver. Blunted autonomic control of the heart may partly be associated with adverse event attributed to cigarette smoking [12].

Manzano *et al*. total of 25 young smokers underwent beat-to-beat analysis of HR. The results show that smoking resulted in acute modifications in HRV indices, characterized by the decrease in the parasympathetic activity and increase in the sympathetic activity similar to our study [13].

Longer-term indexes of HRV (SDANN, SDNN, VLF power) may reflect thermoregulatory, neuroendocrine, circadian, and other, unknown influences. SDNN and total power, although they are measures of total variability, are primarily influenced by longer-term trends in HR and are included with indexes reflecting LTV [16]. All longer-term indexes of HRV are markedly reduced among smoking individuals. However, long time recordings of HRV are needed to provide reliable results for time domain parameters. In our study, only 8 minutes recording of HRV was done, so LF and HF oscillations were more reliable.

Frequency domain of HRV depicts significant changes between the groups. Table 4 shows HF power was significantly decreased in smoking individuals compared to non-smoking individuals. Fig. 5 shows the control group HF mean is compared with smokers in three categories mild, moderate and severe and found that HF is decreased vastly in severe category of smoking compared with mild. LF/HF ratios of smokers and non-smokers were compared in Fig. 6, mean LF/HF ratios tended to be higher in smokers, differences were statistically significant ($p<0.05$) which shows sympathetic overactivity or parasympathetic under activity. LF power reflects both sympathetic and parasympathetic modulation of the HR. In this study, LF power was significantly increased in smoking individuals compared with non-smoking control subjects shown in Table 4 and Fig. 7.

Fumio Kobayashi et al concluded that LF/HF increases significantly within 5 minutes of smoking. Smokers are found to have potent effects of cardiac autonomous modulation. Presence of circadian rhythm observed with sympathomimetic activity during the day and increase in parasympathetic activity during night [14].

To evaluate dose and duration response relationship, quantification of tobacco smoking was done by calculating a smoking index for smokers. Accordingly, we classified the smokers into light, moderate and heavy smokers as per the criteria of the smoking index. It was observed that the HRV parameters of light smokers are not found to be significant when compared to control group. Moderate smokers show significant decrease in Pnn50 and frequency domain parameters such as HF and significant increase in LF, LF/HF of HRV compared with control group, heavy smokers show significant decrease in time domain parameters such as RMSSD, NN50, Pnn50, and frequency domain parameters like HF and significant increase in LF, LF/HF of HRV compared with control group shown in Fig. 6.

CONCLUSION

HRV analysis of smokers and control shows that smoking subjects have an autonomic imbalance suggestive of an increased sympathetic tone or decreased parasympathetic tone. Sympathetic overactivity may lead to cardiovascular disease development in smokers. Heavy smokers are more prone to autonomic dysfunction. This study carried out to predict the autonomic imbalance in smokers will be helpful for planning the novel therapeutic and preventive approaches in the smokers.

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