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Research Article

Study of ECG changes and left ventricular diastolic dysfunction as hemodynamic markers of myocardial stress in chronic smokers

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ABSTRACT

Background: Nicotine being the chief component of cigarette smoke, is a potent inhibitor of the cardiac A type potassium channels, which contributes to the changes in the electrophysiology of heart and affects the cardiac diastolic functions. The present study was undertaken to evaluate the ECG changes, left ventricular diastolic functions and dyslipidemia in chronic smokers.
Methods: 127 healthy male volunteers without any systemic illnesses, drug or alcohol intake, in the age group of 20-60 years, who attended the outpatients department of a tertiary care government hospital were recruited for the study. They were subsequently divided into smoker group consisting of 64 subjects with ≥20 pack years of smoking duration and the non-smoker group consisting of 63 subjects, who were never smokers. All the subjects were evaluated for lipid profile and 2D echocardiography was done to assess the Left Ventricular Ejection Fraction (LVEF). The ECG was recorded for all the subjects and parameters such as the heart rate, the PR interval and the QRS complex and ST interval were assessed in seconds. The QTc (corrected QT interval) was calculated by using Bazet's formula.
Results: The lipid profile of smokers indicated significantly high Total Cholesterol, LDL, VLDL, TG and significantly low levels of HDL in comparison to non-smokers. ($p<0.001$) The ECG and echocardiography analysis showed significant increase in the heart rate and shortening of QRS complex and ST interval along with significant reduction in LVEF ($P <0.001$) in the smokers.
Conclusion: Along with conventional markers of dyslipidemia, shortening of QRS complex, ST segment and reduced LVEF should be considered as markers of myocardial stress in chronic smokers while screening them for risk of coronary artery disease.

Keywords: Smoking, Electrocardiography, Nicotine, Echocardiography, Dyslipidemia

INTRODUCTION

Cigarette smoking is considered as one of the strongest risk factor for cardiovascular morbidity and mortality. Smoking predisposes to atherosclerosis which in turn leads to coronary artery disease, stroke, sudden death, peripheral artery disease, and aortic aneurysm.[1] Smoking has varied effects on the cardiovascular system.[2] The duration and frequency of smoking play an important role in determining the extent of harm caused to the cardiovascular system. The incidence of myocardial infarction is increased to six fold in women and three fold in men who smoke at least 20 cigarettes per day compared to subjects who never smoked.[3,4] Previous studies have stated that nicotine, which is the main component of tobacco, accelerates lipid peroxidation and thus induces atherosclerosis and predisposes to Coronary Artery Diseases (CAD).[5,6] Apart from its atherosclerotic effect, nicotine causes disturbances in the

electrophysiology of heart and may lead to ventricular arrhythmias.[7] The cardiac effects of nicotine are attributed to catecholamines, which are released due to the binding of nicotine to the nicotinic cholinergic gate on the cation channels in receptors (nAchR) throughout the body.[7,8] An electrocardiogram is a simple representation of the electrical activity of the heart muscle during the cardiac cycle.[8] Recording of ECG is one of the easiest, cheap and reliable methods of assessing cardiovascular function. Studies have shown that smoking habbit induces changes in the normal ECG pattern, but the results have been inconsistent. Left ventricular diastolic functions have long been implicated as significant clinical parameter of assessing myocardial damage.[9] In the last few years, interest regarding the effect of smoking on the cardiac diastolic function has increased, and echocardiographic evidence of diastolic dysfunction has been demonstrated during acute cigarette smoking in patients with CAD.[10] While other studies in healthy smokers have shown conflicting results.[11] Hence the present study aimed to evaluate the lipid profile, Left Ventricular Ejection Fraction (LVEF) and electrocardiographic changes in smokers, so as to identify the hemodynamic markers of cardiac stress, to stratify them as high risk for development of CAD.

METHODS

Materials

130 healthy male volunteers, in the age group of 20-60 years, who attended the outpatients department of Gandhi medical college and hospital, Secunderabad, were recruited for the study after obtaining written informed consent from them. They were subsequently divided into two groups based on their history of smoking, as per the World Health Organization's (WHO's) 10th revision of the International Statistical Classification of Diseases and related health problems (ICD-10) criteria of harmful use.[12]

Institutional ethics committee clearance was obtained. This study was conducted over a period of two years. Out of the volunteers, 64 were smokers and 63 were non-smoker subjects.

Three subjects were discarded since they did not meet our selection criteria. Subjects with BMI >30 and those with hypertension, diabetes mellitus, rheumatic heart disease, ischemic heart disease, evidence of left ventricular hypertrophy, systolic dysfunction, wall motion abnormalities, infiltrative diseases or pericardial disease were excluded from the study. The chronic smokers had a mean duration of 18 ± 2.5 pack years of smoking (≥20 pack years of smoking i e 20 cigarettes per day for one year constitutes one pack year)[13] whereas the control group were never smokers. Clinical parameters were documented in a well-designed proforma prior to collection of 10 milliliters of blood from each of these subjects, for investigating the lipid profile

Techniques

Body mass index (BMI)

The body mass index of all the subjects was calculated by the accepted formula: weight (kg)/height (meter)^2.

Lipid profile

Serum Total Cholesterol (TC), triglycerides (TG), High-Density Lipoprotein (HDL), Low Density Lipoprotein (LDL) were done by auto-analyser (Hitachi 912). Very Low Density Lipoprotein (VLDL) was calculated by Friedewald's formula.[14]

Blood pressure

The Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) were recorded by sphygmomanometer in the morning, prior to collection of blood sample. Mean Arterial Blood Pressure (MABP) was calculated with the formula: Diastolic pressure +1/3rd of Pulse pressure (DBP+1/3rdPP).

Heart rate

Recording of pulse was done by palpating the radial artery for full one minute.

ECG recording

ECG recording was carried out in all the 127 subjects after thorough clinical and systemic examinations were done. With the subjects in the resting supine position, a 12 lead electrocardiogram was recorded by using a single channel ECG cardiant (heart view 1200 ECG recorder-manufactured by Brown Dove Healthcare Pvt Ltd). The following parameters were namely, PR interval, QRS complex, ST segment were evaluated in seconds. The QTc (corrected QT interval) was calculated by using Bazet's formula (QT interval/square root of the RR interval).[15]

Conventional 2D echocardiography

Two dimensional M-mode echocardiography was performed in the parasternal long and short axis views and apical two and four chamber views. Left Ventricular Ejection Fraction (LVEF) was estimated according to LV volumes evaluated by biplane method of disks (modified Simpson's rule), according to the criteria provided by the American Society of echocardiography.[16]

Statistical analysis

The data was expressed as mean ± standard deviation. The results which were obtained were statistically analyzed by using the student's 't' test. The probability (P value) was calculated. A P value of <0.001 was taken as

highly significant, a P value of <0.05 as significant and a P value of >0.05 as non- significant.

RESULTS

The comparison of baseline data indicated no significant change in SBP and DBP among both the groups. The BMI of smokers was found to be significantly lower (P <0.05) than that of non-smokers (Table 1). The lipid profile of smokers indicated significantly high total cholesterol, LDL, VLDL, TG (P <0.001) and significantly low levels of HDL in comparison to non-smokers (Table 2). Upon clinical examination, all the study subjects were found to be in sinus rhythm. Heart rate showed a statistically significant increase in smokers group compared to non-smokers (P <0.001). The ECG analysis suggested significant shortening of QRS complex (P <0.05) and ST segment (P <0.001) in smokers (Table 3, Figure 1). On echocardiographic examination, no wall motion abnormalities, or clinically significant valvular regurgitation were detected in any of the study subjects. The echocardiography analysis suggested significant reduction (P <0.001) of the Left Ventricular Ejection Fraction (LVEF) in smokers group (Table 3).

Table 1: Comparison of baseline parameters across the groups.

	Nonsmokers N=63	Smokers N=64	P value
Age (years)	51.9 ± 1.2	52.3 ± 1.5	0.104 (NS)
BMI (kg/m^2)	19.79 ± 1.87	19.12 ± 1.13	0.03
SBP (mm of Hg)	128 ± 12.59	130.81 ± 20.1	0.347 (NS)
DBP (mm of Hg)	80.25 ± 4.39	79.34 ± 6.95	0.380 (NS)
MABP (mm of Hg)	96 ± 6.09	95.83 ± 9.35	0.903 (NS)

P value >0.05 - Not significant (NS),*P value <0.05

Table 2: Comparison of lipid profile among both the groups.

	Nonsmokers N=63	Smokers N=64	P value
Total cholesterol (mg%)	162.65 ± 16	235.1 ± 33.23	0.00
HDL (mg%)	46.07 ± 6.98	36.48 ± 6.16	0.00
LDL (mg%)	97.1 ± 10.7	189.49 ± 27.95	0.00
VLDL (mg%)	22.73 ± 5.72	31.63 ± 3.79	0.00
TG (mg%)	115.04 ± 26. 57	158.45 ± 18.91	0.00

*P value<0.05, **P value <0.001

Table 3: Parameters of ECG analysis and LVEF in smokers and non-smokers.

	Non-smokers (n-64)	Smokers (n-64)	P value
Heart rate (beats/ min)	70.35 ± 7.37	76.1 ± 9.06	0.00
P-R interval (Secs)	0.14 ± 0.024	0.15 ± 0.036	0.063 (NS)
QRS complex (Secs)	0.09 ± 0.026	0.08 ± 0.018	0.01
QT interval (Secs)	0.39 ± 0.043	0.37 ± 0.041	0.177 (NS)
QTc interval (Secs)	0.36 ± 0.04	0.35 ± 0.039	0.157 (NS)
ST interval (Secs)	0.32 ± 0.02	0.29 ± 0.01	0.00
LVEF (%)	64 ± 3.7	59 ± 2.8	0.00

P value >0.05 - Not significant (NS),*P value <0.05,**P value <0.001

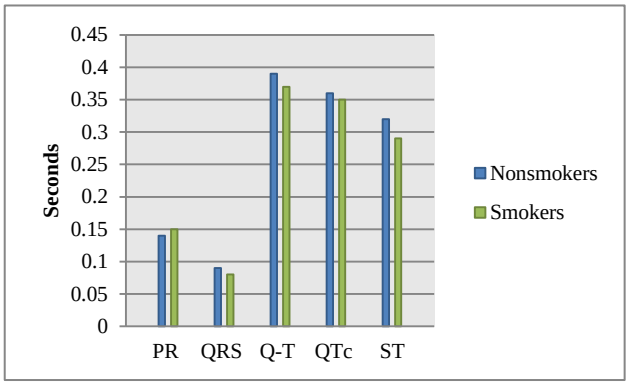

Figure 1: Comparison of PR, QRS, QT, QTc and ST intervals among smokers and non-smokers.

DISCUSSION

Smoking is a potent risk factor for cardiovascular morbidity and mortality by causing atherosclerosis. [17] In our study, while comparing the base line clinical parameters we did not observe any significant difference in terms of systolic, diastolic and mean arterial blood pressure among both the groups. However, we observed significantly lower body mass index in smokers than non-smokers, (P <0.05) which was in concurrent with earlier studies done by Chieloro et al. suggesting smokers to have a lower BMI than non-smokers in health as well as disease.[18] Cross-sectional studies indicate that mean BMI tends to be lower in smokers than non-smokers because of the metabolic and possible acute anorexic effects induced by nicotine.[19]

Dyslipidemia is another factor associated with smoking.[20] While comparing the lipid profile, it was observed that the total cholesterol, VLDL, TG were increased significantly (P <0.001) (Table 2) and HDL was significantly decreased (P <0.001) in smokers whereas no

significant difference was observed in LDL. Nicotine causes an increased activity of HMG-CoA reductase and decreased lipoprotein lipase activities, resulting in elevated levels of total cholesterol and TG, LDL, and VLDL.[21] In addition, nicotine stimulates the sympathetic adrenal system, which leads to increased lipolysis. According to McCall et al. the reduced HDL level in smokers is due to its increased catabolism and the inactivation of the Lecithin-Cholesterol Acyl Transferse (LCAT) system.[22]

In the present study, heart rate was observed to be significantly increased in smokers than non-smokers. (P <0.001) (Table 3). This can be attributed to the fact that nicotine stimulates release of endogenous adrenergic neuro-transmitters and exerts a positive chronotropic effect.[23] In smokers, nicotine appears to induce increased sympathetic discharge and stimulation of adrenal medulla leading to copious secretion of the adreno-medullary hormones and thereby increasing the plasma levels of epinephrine and nor-epinephrine.[23] As a result, there is a positive chronotropic effect exerted by nicotine resulting increase in the resting heart rate of smokers. While analysing the ECG waves of smokers and non-smokers, we observed significantly shortened QRS complex (P <0.05) and shortened ST interval (P <0.001) in smokers than non-smokers (Figure 1).

We did not observe any significant change in QT, QTc and PR interval among both the groups. Nicotine mediates the changes in the normal electrophysiology of heart, as it is a potent inhibitor of the cardiac A type potassium channels, which contributes to the resting membrane potential of myocardiocytes.[24] Nicotine facilitates a conduction block and a re-entry of cations, thus causing electrophysiological disturbances and increasing the vulnerability to ventricular fibrillation.[25] The shortened QRS complex and ST interval indicate that there is incomplete ventricular filling phase during which the coronary supply occurs. This may lead to an insufficient myocardial perfusion, and may invite episodes of myocardial ischemia.[25] Thus shortened QRS complex and ST interval in smokers warn of predisposing to episodes of arrhythmia. In a similar study of ECG changes in smokers done by Venkatesh G et al., (2010) a significant shortening of the QRS complex was observed, whereas the other waves did not show much change.[26] Our study is concurrent with that of Karjalainen et al., who have reported significantly shortened QRS complex and ST interval and have suggested that a shortened ST interval observed in smokers is a risk factor for ischemic heart disease.[27] However our study does not agree with Devi et al., (2013) who have reported significantly reduced ST interval, but widened QRS complex and shortened QTc interval in smokers.[28] The differences in the findings of previous studies may be due to differences in the inclusion criteria such as duration of smoking, smoking intensity and dyslipidemia status of subjects participating in the study.

The echocardiography analysis revealed LVEF, to be significantly lower in smokers then non-smokers (P <0.001) (Table 2). The reduced LVEF is indicative of myocardial stress and may lead to impaired myocardial perfusion predisposing the smokers to CAD. Our findings are concurrent with that of Ambrose et al who have also reported LVEF to be significantly lower in chronic smokers indicating reduced myocardial contractility thus increasing the risk of CAD.[1] Also Alam et al. in their study have reported that smokers to have significantly reduced LVEF and it may predispose to episodes of myocardial ischemia in them.[10] Thus the present study suggest that chronic cigarette smoking of more than 20 pack years causes impairment in left ventricular diastolic function and disturbances in the electrophysiology of heart, thus increasing the risk of mortality from coronary artery disease.

CONCLUSION

Along with conventional markers of dyslipidemia and reduced LVEF, the shortening of ST interval and QRS complex should be considered as hemodynamic markers of myocardial stress while screening apparently healthy smokers for the risk of CAD and should be used by the physician to counsel the smokers to stop smoking as early as possible.

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