Original Article

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Physiology Section

Evaluation of Dyslipidaemia and Echocardiographic Markers of Myocardial Contractility in Smokers with Ischaemic Heart Disease

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ABSTRACT

Introduction: Cigarette smoking is responsible for dyslipidaemia and haemodynamic disturbances.

Aim: The present study was conducted to evaluate the parameters of dyslipidaemia and left ventricular ejection fraction in smokers with Ischemic Heart Disease (IHD).

Materials and Methods: Total number of study subjects included 327 males, which included 127 healthy subjects and 200 subjects admitted as IHD patients under the inclusion criteria meant for categorizing chronic smokers. They were subsequently divided into smoker and non-smoker groups and evaluated for lipid profile and 2D echocardiography.

Results: The parameters of lipid profile revealed significant difference ($p<0.001$) in all lipid parameters except HDL among non-smokers vs smokers in both patient and control groups. The echocardiography analysis suggested significantly (<0.001) reduced ejection fraction in patients with smoking habit compared to without smoking habit.

Conclusion: Chronic smokers with history of ≥15 pack years should undergo screening for IHD by timely evaluation of ejection fraction along with estimation of lipid profile.

Keywords: Ejection fraction, Lipid profile, Nicotine

INTRODUCTION

Cigarette smoking accelerates lipid peroxidation and thus, induces atherosclerosis and predisposes to Coronary Artery Disease (CAD) [1]. Nicotine present in the cigarette apart from the atherosclerotic effect, leads to changes in the electrophysiology of heart and may cause ventricular arrhythmias. These cardiac changes are caused due to the release of catecholamines from binding of nicotine to nicotinic Acetylcholinergic Receptors (nAchRs) throughout the body. [2]. In recent years, the role of ventricles in haemodynamic function of the heart has been more emphasized. Impairment of relaxation, the early phase of ventricular diastole, is the first stage of diastolic dysfunction. Left Ventricular (LV) diastolic function can be determined by Doppler echocardiography-derived Mitral Valve Flow (MVF) velocities [3]. Left ventricular diastolic dysfunctions have long been implicated as significant clinical parameter of assessing myocardial damage [4]. In recent times, the effects of smoking on the isolated diastolic function has been an interesting subject for research work, and echocardiographic changes of diastolic dysfunction have been seen in CAD patients during acute cigarette smoking. [5]. The left ventricular diastolic function can be assessed by recording the MVF pattern such as, early phase (E-wave), late phase (A-wave), De-acceleration Time (DT) and Iso-Volumetric Relaxation Time (IVRT) [6]. The LV diastolic dysfunction usually precedes the systolic dysfunction and may cause clinical signs of congestive heart failure in smokers along with CAD [7]. Studies have reported early changes of LV diastolic dysfunction in chronic smokers [7]. Hence, in the present study, the LV diastolic functions are assessed by determining the MVF in young healthy smokers, and compared with healthy controls, patients with smoking habit and without smoking habit, so as to identify the haemodynamic markers of cardiac stress in them.

MATERIALS AND METHODS

The present observational case control study included 327 male subjects, consisting of 127 healthy subjects and 200 consecutively admitted IHD patients in the intensive cardiac care unit of Cardiology Department (ICCU, Gandhi Medical College and Hospital, Secunderabad, India) over the period from January 2013 to July 2014. All the IHD patients were diagnosed according to the following diagnostic criteria: chest pain lasting for >3 hours, ECG changes (ST elevation >2 mm in at least two leads) and elevation of enzymatic activity of serum creatinine phosphokinase and aspartate aminotransferase. The evaluation of antioxidant enzymes and ACE gene I/D polymorphism studies were carried out from this sample and are already published [8,9]. Each of the main groups were subsequently categorized as smokers and non-smokers based on the history of smoking. i.e., ≥15 pack years of smoking (20 cigarettes per day for one year constitutes one pack year) [10]. The group of IHD patients were divided into 2 subgroups consisting of 100 non-smokers and 100 smokers, the healthy group consisted of 64 smokers and 63 non-smokers. The mean ages of investigated human groups were sufficiently close. The healthy smokers and non-smokers were of mean age 48±1.5 years; the sub-group of smoker IHD patients were 54±2.5 years and group of non-smoker patients were 50.4±2.1 years of age.

The study was approved by institutional ethics committee. Informed consents were obtained from all the patients or relatives, before collection of blood samples. Patients with renal disease, hepatic disease or any other neurological disorders were excluded from the study. The following investigations were carried out in the patient and control group:

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 equation [11].

Echocardiography: A study of 2-dimensional M mode echocardiography and Doppler echocardiography was performed by the qualified technician under the supervision of the cardiologist. Two-dimensional and Doppler echocardiographic examinations were

performed with an ultrasonographic system (Philips iE 133 echo Doppler) equipped with multifrequency transducer. Left Ventricular Ejection Fraction (LVEF) was calculated from apical two and four chamber views. From the apical four chamber view, the transmitral flow at the level of the leaflet tips was obtained and following parameters were defined: the maximal flow velocity (centimeters per second) of MVF early phase (E) and the maximal velocity of MVF latephase (A), the MVF E/A ratio, and De-acceleration Time (DT) [12]. From the apical five-chamber view, the simultaneous recording of the aortic and mitral flows were evaluated and the IVRT, the time interval between aortic valve closure and mitral valve opening was measured [13].

STATISTICAL ANALYSIS

The data were expressed as mean±standard deviation. The results which were obtained were statistically analysed by using student t-test and one-way ANOVA followed by post-hoc tukey test by using SPSS software version 19.0. A "p"-value of <0.05 was taken as significant.

RESULTS

The baseline data of control and patient group is given in [Table/Fig-1,2] respectively. [Table/Fig-1] shows that the systolic blood pressure is slightly high in smokers whereas the diastolic blood pressure is nearly the same in both smokers and non-smokers. A similar trend was seen in patients with IHD where both smokers and non-smokers had a history of DM but here also the systolic was on higher side in comparison to diastolic blood pressure in smokers than in non-smokers. The lipid profile of smokers and non-smokers is described in [Table/Fig-3] which shows than even though smokers from control group had high TG, a low HDL and high LDL these were comparatively varying when compared with smokers having history of IHD, where the values of TG were higher, HDL were lower and LDL were higher when compared with smokers from control group. The lipid profile of smokers and non-smokers is described in [Table/Fig-3]. The multiple comparison of the parameters of lipid profile revealed significant difference (p<0.001) in all lipid parameters except HDL among non-smokers vs smokers in both patient and control groups.

Parameters	Non-smokers (n=63)	Smokers (n=64)
Age (years)	48.6±1.5	49.1±1.4
Pack years of smoking	Nil	14.62±1.3
Diabetes Mellitus (%)	Nil	Nil
SBP (mm of Hg)	128±12.59	130.81±20.1
DBP (mm of Hg)	80.25±4.39	79.34±6.95

[Table/Fig-1]: Baseline data and demography of controls.
SBP-Systolic blood pressure, DBP-Diastolic blood pressure, ** p<0.001

Parameters	Non-smokers(n=100)	Smokers (n=100)
Age (years)	54±2.5	50.4±2.1**
Pack years of smoking	nil	15.2±1.5
Diabetes Mellitus (%)	34.3±2.8	33.8±3.1
SBP (mm of Hg)	128.78±10.31	131.34±16.93
DBP (mm of Hg)	80.14±4.22	79.66±6.7

[Table/Fig-2]: Baseline data and demography of IHD patients.
CK-MB-Creatine kinase MB, SBP-Systolic blood pressure, DBP-Diastolic blood pressure, * * p<0.001

Parameters	Controls		Patients	
	Non-smokers (n=63)	Smokers (n=64)	Non-Smokers (n=100)	Smokers (n=100)
TC (mg/dl)	162.65±16£**	235.1± 33.23‡**	209.45± 18.44†**	236.5±2 9.42§**
HDL (mg/dl)	46.07±8.98£**	42.48±7.16‡ **	36.03±4.85†**	34.92±5.38
LDL (mg/dl)	97.1±10.7£**	189.49± 27.95‡ **	156.09± 23.08† **	171.04± 31.93§**
VLDL (mg/dl)	22.73±4.32£**	31.63±3.79‡ **	25.83±3.83† **	32.29±4.19§**
TG(mg/dl)	115.04± 22.47£**	158.45± 28.91‡**	130.1± 23.53†**	161.39± 18.82§**

[Table/Fig-3]: Comparison of serum lipid profile between the patient and control groups.
TC-Total cholesterol, HDL- High density lipoproteins, LDL- Low density lipoproteins, VLDL- Very low density lipoproteins, TG-Triglycerides, £ Control nonsmoker vs Control smoker, ‡ Control smoker vs Patient non-smoker, † Control nonsmoker vs Patient nonsmoker, §Patient smoker vs Patient nonsmoker. * p<0.05, * *p<0.001

	Controls		Patients	
	Non-smokers (n=63)	Smokers (n=64)	Non-smokers (n=100)	Smokers (n=100)
MVF-E (cm/s)	65.55± 9.71	65.9±9.2	66.7±10.71	67.33±10.41
MVF-A(cm/s)	48.15±8.5£*	52.29± 7.43	53.19± 9.86†*	53.32± 10.1
E/A ratio	1.34± 0.17£**	1.21± 0.19	1.19± 0.18†**	1.2± 0.19
DT(milli sec)	196.28± 25.66£**	218.5± 28.5	220.9± 24.62†**	224.45± 23.59
IVRT(milli sec)	98.4± 13.47£**	106.44± 18.3‡*	112.33± 15.9†**	114.32± 16.4
EF%	64± 6.7£*	60±8.12‡**	54.92± 5.05†**	49.83± 4.8§**

[Table/Fig-4]: Analysis of echocardiography parameters in IHD patients and controls.
MVF-Mitral valve flow, E- Early wave, A-Late wave, DT- De-acceleration time, IVRT-Isovolumetric relaxation, EF-Ejection fraction, £Control nonsmoker vs Control smoker, ‡ Control smoker vs Patient non-smoker, †Control non-smoker vs Patient non-smokers §Patient smoker vs Patient non-smoker, * p<0.05, * * p<0.001

The echocardiography analysis of patient group and control group is described in [Table/Fig-4]. On echocardiographic examination, no wall motion abnormalities, or clinically significant valvular regurgitation were detected in any of the study subjects. The echocardiography analysis suggested significantly (p< 0.05) prolonged mitral A-wave velocity of control smokers than control non-smokers. Also, the mitral A-wave velocity was significantly increased in non-smoking patients (p<0.05) in comparison to control smokers. The mean E/A ratio of smokers was observed to be decreased significantly (p<0.001) when compared to non-smokers in the control group whereas no such difference was observed between the smokers and non-smokers of control group. The DT was observed to be significantly (p<0.001) enhanced in control smokers compared to patient smokers. Also, the DT was significantly higher (p<0.001) in non-smoking patients than control non-smokers. However, no significant difference was observed in DT between patients with and without smoking habit. The IVRT was observed to be enhanced significantly (p<0.001) in control smokers when compared to control non-smokers and in patient non-smokers when compared to control non-smokers (p<0.001). The LVEF was significantly lower (p<0.001) in smokers than non-smokers of control group as well as patient group.

DISCUSSION

Cigarette smoke exposure is an important cause of cardiovascular morbidity and mortality. In the present study, we observed that the mean age at diagnosis of IHD is 50.47±5.13 years in smokers which is, significantly lower in comparison to non-smokers (p<0.001). The present study supports that of Panwar B et al., who has reported association of smoking with lower age of onset and higher mortality from IHD in Indian smokers [14]. While comparing the lipid profile, except the good cholesterol (HDL), which was observed to be significantly decreased in smokers, all other lipid parameters such as TC,LDL,VLDL,TG were significantly high among the smokers in

comparison to non-smokers in control group as well as in patient group (p<0.001) [Table/Fig-3]. However, we did not observe any significant difference in HDL levels among the smoker patient's vs non-smoker patients, which may be due to other associated lifestyle factors like diet, physical activity, exercise etc., influencing the lipid metabolism [15]. The HDL levels were observed to be significantly decreased in controls with smoking habit compared to without smoking habit. Our findings are suggestive of the fact that cigarette smoking promotes atherosclerosis and dyslipidaemia [15].

The echocardiography analysis in the present experiment did not show any significant differences in the echocardiography parameters except for EF. The EF was significantly (<0.001) reduced in smoker patients in comparison to non-smoker patients [Table/Fig-4] which is already published [16]. While evaluating the echocardiography findings in healthy controls, it was observed that, the control smokers presented with significantly (p<0.001) prolonged DT, increased velocity of A-wave, reduced E/A ratio and increased IVRT compared to non-smokers [Table/Fig-4].

Stork T et al., have evaluated the impact of acute smoking on echocardiography changes and suggested that smoking causes a significant decrease in velocity of E-wave, increase in A-wave and rise of left ventricular filling [4]. However we could not evaluate the acute effects of smoking in patients as it involved ethical issues. These findings suggest that, the decrease of coronary blood flow due to smoking may cause an imbalance between myocardial oxygen demand and supply for the energy-consuming process of myocardial repolarization, and thus impairs LV diastolic function [4,17]. These findings are concurrent with that of Ambrose JA and Barua SR., who have also reported EF to be significantly lower in chronic smokers indicating reduced myocardial contractility, thus increasing the risk of CAD [18]. Reports on LV diastolic function in healthy smokers are sparse. According to Voutilainen S et al., no significant difference was noticed in LV diastolic functions between smokers and non-smokers in a rather non-uniform group of 93 healthy persons aged 11 to 91 years [19]. According to Alam M et al., smokers have a significantly reduced LVEF and it may predispose to episodes of myocardial ischemia in them [5].

LIMITATION

The study was conducted on relatively smaller sample size taken from a limited geographical area. Thus, a study with larger sample size is warranted to further strengthen the present inferences.

CONCLUSION

Thus, the present study concludes that smokers with history of >15 pack years should be screened for risk of IHD by timely evaluation of reduced ejection fraction, along with evaluation of dyslipidaemia irrespective of the age and other risk factors.

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