National Journal of Physiology, Pharmacy and Pharmacology

RESEARCH ARTICLE

Impact of chronic smoking on lipid peroxidation and electrocardiogram in ischemic heart disease patients

Sandhya Metta[1], Umesh G Balgi[1], Shruti Mohanty[2], Archana A Dharwadkar[2]

[1]Department of Physiology, Kamineni Institute of Medical Sciences, Narketpally, Nalgonda, Telangana, India, [2]Department of Biochemistry, Kamineni Institute of Medical Sciences, Narketpally, Nalgonda, Telangana, India

Correspondence to: Umesh G Balgi, E-mail: balgi.umesh@gmail.com

Received: June 01, 2017; **Accepted:** June 16, 2017

ABSTRACT

Background: Cigarette smoking is one of the prime contributing factors for atherosclerosis. Chronic cigarette smoking causes disturbances in the electrophysiology of heart and may lead to ventricular arrhythmias. Furthermore, cigarette smoke produces oxidative stress by generating free radicals which is responsible for lipid peroxidation and atherosclerosis. **Aims and Objectives:** The present study is aimed at evaluating the electrocardiographic (ECG) changes and plasma malondialdehyde (MDA) levels in smokers suffering from ischemic heart disease (IHD). **Materials and Methods:** About 327 male subjects, consisting of 127 healthy subjects and 200 consecutively admitted IHD patients were enrolled for this study and were subsequently divided into two subgroups as smokers and non-smokers consisting of 100 non-smokers and 100 smokers, based on the history of smoking. The healthy control group consisted of 64 smokers and 63 non-smokers. All the subjects underwent ECG recording and evaluation of plasma MDA levels. **Results:** 68% of IHD patients had typical ST elevation type of ECG, and out of these, 74% were smokers and 62% were non-smokers. The analysis of normal ECG waves of control group indicated significantly shortened QRS complex ($P < 0.001$) and shortened ST interval ($P < 0.001$) in smokers than non-smokers. The plasma MDA levels were observed to be highly significant ($P < 0.001$) in control smokers and patient smokers in comparison to control non-smokers and patient non-smokers, respectively. **Conclusion:** In chronic healthy smokers, the QRS complex and ST segment were found to be shortened indicating incomplete ventricular relaxation indicating that the smokers are at higher risk for greater myocardial damage. Furthermore, the greater lipid peroxidation indicated by higher MDA levels in smokers irrespective of the presence of IHD predisposes them to higher risk of atherosclerosis and higher mortality from IHD.

KEY WORDS: Electrocardiogram; Smoking; Ischemic Heart Disease; Lipid Peroxidation

INTRODUCTION

Cigarette smoking has varied effects on the cardiovascular system.[1] The duration and frequency of smoking play an important role in determining the extent of harm caused to the cardiovascular system. 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 disease (CAD).[2] Smoking causes prooxidant/antioxidant imbalance which elevates oxidative stress, accompanied by an increase of lipid peroxidation and vasomotor dysfunction for the initiation and progression of atherosclerosis.[1] The quinone-hydroquinone radical complex from the cigarette tar causes redox cycling and generates copious superoxide radicals, which further produces hydrogen peroxide and hydroxyl radicals causing

Access this article online	
Website: www.njppp.com	Quick Response code
DOI: 10.5455/njppp.2017.7.0619816062017	

enhanced lipid peroxidation in smokers.[2] Apart from its atherosclerotic effect, nicotine causes disturbances in the electrophysiology of heart and may lead to ventricular arrhythmias.[3] The cardiac effects of nicotine are attributed to catecholamines, which are released due to the binding of nicotine to the nicotinic acetylcholinergic receptors (nAchR) throughout the body.[4] An electrocardiogram is a simple representation of the electrical activity of myocardium during the cardiac cycle.[3] Recording of electrocardiogram (ECG) is one of the easiest, cheap, and reliable methods of assessing cardiovascular function. The studies on ECG changes in young smokers have been conflicting and are in need of further study.[5] According to Gidding et al. in smokers, there is a positive association between baseline major Q-waves and smoking duration in pack years which supports the idea that increased CVD risk related to long-term smoking can be detected by the 12-lead ECG. Nicotine is considered to increase the vulnerability to ventricular fibrillation.[6] Since nicotine is a potent inhibitor of the cardiac A-type potassium channels, it may contribute to the changes in the cardiac electrophysiology and also may induce arrhythmias.[7] Since there are fewer studies on effect of smoking habit on lipid peroxidation and ECG pattern, the present study was undertaken to evaluate the lipid peroxidation by estimating the malondialdehyde (MDA) levels in smokers and non-smokers and compare the ECG changes in chronic healthy smokers as well as chronic smokers suffering from ischemic heart disease (IHD) to identify the hemodynamic markers of cardiac stress leading to development of CAD.

MATERIALS AND METHODS

The present 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 January 2013-July 2014. All the IHD patients were diagnosed according to the following diagnostic criteria: Chest pain lasting for > 3 h, ECG changes (ST elevation >2 mm in at least two leads), and elevation of enzymatic activity of serum creatine phosphokinase and aspartate aminotransferase. The group of healthy subjects was recruited from the patient relatives and outpatient wards of other clinical departments, after they were screened for hypertension, diabetes, renal, or neurological conditions that might interfere with our study. Each of the main groups was subsequently categorized as smokers and non-smokers based on the history of smoking (≥15 pack years of smoking, i.e., 20 cigarettes per day for 1 year constitutes one pack year).[8] 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 subgroup of the smoker with IHD patients was 54 ± 2.5 years, and group of non-smoker patients was 50.4 ± 2.1 years of age.

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

Blood Pressure

The systolic blood pressure and diastolic blood pressure (DBP) were recorded by sphygmomanometer in the morning, before collection of blood sample. Mean arterial blood pressure was calculated with the formula: Diastolic pressure+one-third of pulse pressure (DBP+1/3rd PP).

Heart Rate

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

Thiobarbituric Acid Reactive Substances Assay

Plasma MDA levels were determined by the method of Richard et al., using the Cayman kits (item no.10009055, Ann Arbor, MI 48108, USA).[9] In this method after centrifuging the blood at 1,000 g for 10 min at 40°C, the top yellow plasma layer was pipetted off. The MDA-thiobarbituric acid (TBA) adduct formed by the reaction of MDA and TBA under high temperature (90-1000°C), and acidic condition was measured colorimetrically at 530-540 nm.

ECG Recording

ECG recording was carried out in all the 327 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 using Bazett's formula (QT interval/ square root of the RR interval).[10]

RESULTS

The comparison of HR, BP, and plasma MDA levels in patients group is described in Table 1. The comparison of parameters of BP, HR, and plasma MDA levels in the control smokers and non-smokers is given in Table 2. There was a significant increase observed in HR while comparing between smokers and non-smokers ($P < 0.001$). The plasma MDA levels were observed to be increased significantly ($P < 0.001$) (Tables 1

Table 1: Comparison of BP, HR, and plasma MDA levels in IHD patient group

Parameters	Non-smokers (*n*=100)	Smokers (*n*=100)
SBP (mm of Hg)	128.78±10.31	131.34±19.93
DBP (mm of Hg)	80.14±4.22	79.66±6.7
PP (mm of Hg)	38.7±5.21	39.6±4.78
MABP (mm of Hg)	96.29±13.53	96.14±9.17
HR (beats/min)	71.52±8.42	72.2±7.16
MDA levels (nmol/dl)	5.03±0.72	6.1±0.72**

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, PP: Pulse pressure, MABP: Mean arterial blood pressure, HR: Heart rate, MDA: Malondialdehyde, BP: Blood pressure, IHD: Ischemic heart disease, ***P*<0.001

Table 2: Comparison of BP, HR, and plasma MDA levels in controls

Parameters	Non-smokers (*n*=63)	Smokers (*n*=64)
SBP (mm of Hg)	128.7±12.59	130.81±20.1
DBP (mm of Hg)	80.25±4.39	79.34±6.95
PP (mm of Hg)	39.8±5.87	40.2±6.2
MABP (mm of Hg)	96±6.09	95.83±9.35
HR (beats/min)	70.35±7.37	76.1±9.06**
MDA levels (nmol/dl)	2.9±0.43	3.1±0.49**

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, PP: Pulse pressure, MABP: Mean arterial blood pressure, HR: Heart rate, MDA: Malondialdehyde, BP: Blood pressure,***P*<0.001

and 2) in smokers as compared to non-smokers in the control group as well as in the patient group.

The type of ECG recordings observed in the patient group is given in Table 3. The presentation of ECG recordings in IHD patients indicated that 74% had typical ST elevation in the patient smokers, whereas in case of non-smoker patients, 62% were admitted with ST elevation MI. Out of 200 patients, 136 (68%) patients represented with ST elevation ECG, whereas 64 patients (32%) presented with ST depression.

The comparison of various components of normal ECG analysis between smokers and non-smokers of the control group is described in Table 4. The analysis of various components of ECG in control smokers and control non-smokers revealed significant shortening of QRS complex ($P < 0.001$) and ST interval ($P < 0.001$) in smokers.

DISCUSSION

While comparing the BP and HR in patient as well as control groups, the control group presented with significantly increased HR in smokers than non-smokers ($P < 0.00$) (Table 2) which is attributed to nicotine.[11] The plasma MDA levels were observed to be increased significantly ($P < 0.001$) (Tables 1 and 2) in smokers as compared to non-smokers in

Table 3: Types of abnormal ECG patterns in IHD patients

Parameters	Smokers (%)	Non-smokers (%)	Total
ST elevation MI	54 (74)	46 (62)	136
ST depression MI	41 (24)	59 (35)	59
ST depression with T-wave inversion	40 (2)	60 (3)	5
Total number patients	100	100	200

IHD: Ischemic heart disease, ECG: Electrocardiographic

Table 4: Analysis of normal ECG in control smokers and non-smokers

Parameters	Non-smokers (*n*=63)	Smokers (*n*=64)
P-R interval (secs)	0.14±0.024	0.15±0.04
QRS complex (secs)	0.09±0.016	0.08±0.01*
QT interval (secs)	0.39±0.043	0.38±0.041
QTc interval (secs)	0.36±0.04	0.35±0.039
ST interval (secs)	0.32±0.02	0.29±0.01**

**P*<0.05, ***P*<0.00, ECG: Electrocardiographic

the control group as well as in the patient group, indicative of enhanced lipid peroxidation in smokers. The analysis of normal ECG waves of control smokers and non-smokers indicated significantly shortened QRS complex ($P < 0.001$) and shortened ST interval ($P < 0.001$) in smokers than non-smokers (Table 4) indicating incomplete ventricular filling. However, there was no significant change observed in QT, QTc, and PR intervals among both the groups. The ECG analysis of smokers and non-smokers of the patient group was suggestive of characteristic ECG findings (diagnostic criteria) typical of AMI as they manifested with ST elevation or ST depression type of ECG recordings. ST elevation MI was observed to be more prevalent in smokers than in non-smokers particularly at relatively younger age, i.e., <60 years. The findings of the present study are concurrent with that of a recent study by Sharma et al., who have reported higher (72%) prevalence of ST elevation MI in smoker IHD patients in comparison to non-smoker IHD patients.[12]

The increase in HR in smokers may be due to nicotine-mediated increase in the sympathetic discharge and stimulation of adrenal medulla leading to increase in the plasma levels of epinephrine and norepinephrine.[11,13] Our findings of significantly elevated MDA levels in smokers of both control and patient groups are suggestive of high lipid peroxidation in smokers. The present results are in concurrent with that of Lykkesfeldt et al. who have reported that smoking induces lipid peroxidation significantly and thereby increases the plasma levels of MDA in comparison to non-smokers.[14,15] The shortened QRS complex and ST interval indicate that there is an 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.[6] It has been assumed that nicotine facilitates a conduction block and a reentry of cations, thus causing electrophysiological disturbances and increasing the vulnerability to ventricular fibrillation.[6]

The present 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 IHD.[16] However, the present study does not agree with Devi et al., who have reported significantly reduced ST interval but widened QRS complex and shortened QTc interval in smokers.[17] 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.

CONCLUSION

Thus, the present study concludes that chronic smoking is associated with increased lipid peroxidation which may predispose smokers to IHD. The ST elevation MI is more prevalent in chronic smokers with >15 years of smoking history indicating that the smokers are at higher risk for greater myocardial ischemia and higher mortality from IHD. In chronic healthy smokers, the QRS complex and ST segment of ECG were found to be shortened indicating incomplete ventricular relaxation.

ACKNOWLEDGMENTS

The authors would like to thank Dr. D Joyarani, Professor of Physiology, Gandhi Medical College, Secunderabad, for her immense guidance and support throughout the study period. They are also thankful to faculty of the Department of Cardiology, Gandhi Medical College for their support with clinical resources.

REFERENCES

1. Ambrose JA, Barua SR. The pathophysiology of cigarette smoking and cardiovascular disease, an update. J Am Coll Cardiol. 2004;43:1731-7.
2. Witztum JL. The oxidation hypothesis of atherosclerosis. Lancet. 1994;344:793-35.
3. Chevalier HJ, Hunnigh C, Bandilla B, Hanel JW. Effect of high doses of nicotine in pig: Changes of the electrocardiogram. Basic Res Cardiol. 1976;71:68-75.
4. Stewart PM, Cetterall JR. Chronic nicotine ingestion and atrial fibrillation. Br Heart J. 1985;54:222-3.
5. Gidding SS, Xie X, Liuk K, Manolio T, Flack JM, Gardin JM, et al. Cardiac function in smokers and non-smokers: The CARDIA study. J Am Coll Cardiol. 1995;26:211-6.
6. Yashima M, Ohara T, Cao JM, Kim YH, Fishbein MC, Mandel WJ, et al. Nicotine increases ventricular vulnerability to fibrillation in hearts with healed myocardial infarction. Am J Heart Circ Physiol. 2000;278(6):124-33.
7. Huizhenwang HS, Baofeng Y. Nicotine is a potent blocker of the cardiac a-type K+Channels. Circulation. 2000;102:1165-71.
8. Prignot J. Quantification and chemical markers of tobacco-exposure. Eur J Respir Dis. 1997;70:1-7.
9. Richard MJ, Portal B, Meo J, Coudray C, Hadjian A, Favier A, et al. Malondialdehyde kit evaluated for determining [18] plasma and lipoprotein fractions that react with thiobarbituric acid. Clin Chem. 2009;38(5):704-9.
10. Bazett HC. An analysis of the time-relations of electrocardiograms. Heart. 1920;7:353-70.
11. Sandhya M, Satyanarayana U, Joyarani D. Study of ECG changes and left ventricular diastolic dysfunction as hemodynamic markers of myocardial stress in chronic smokers. Int J Res Med Sci. 2015;3:588-92.
12. Sharma R, Bhairappa S, Prasad SR, Manjunath CN. Clinical characteristics, angiographic profile and in hospital mortality in acute coronary syndrome patients in south Indian population. Heart India. 2014;2:65-9.
13. Hering D, Somers VK, Kara T. Sympathetic neural responses to smoking are age dependent. J Hypertens. 2006;24:691-5.
14. Lykkesfeldt J, Viscovich M, Poulsen HE. Plasma malondialdehyde is induced by smoking: A study with balanced antioxidant profiles. Br J Nutr. 2004;92:203-6.
15. Kashinakunti SV, Kollur P, Kallaganada GS, Rangappa M, Ingin JB. Comparative [28] study of serum MDA and vitamin-C levels in non-smokers, chronic smokers and chronic smokers with acute myocardial infarction in men. J Res Med Sci. 2011;16(8):993-8.
16. Karjalainen J, Reunanen A, Ristola P, Viitasalo M. QT interval as a cardiac risk factor in a middle aged population. Heart. 1997;77(6):543-8.
17. Devi MR, Arvind T, Saikumar P. ECG changes in smokers and non-smokers: A comparative study. J Clin Diagn Res. 2013;7(5):824-6.

How to cite this article: Metta S, Balgi UG, Mohanty S, Dharwadkar AA. Impact of chronic smoking on lipid peroxidation and electrocardiogram in ischemic heart disease patients. Natl J Physiol Pharm Pharmacol 2017;7(11):1182-1185.

Source of Support: Nil, **Conflict of Interest:** None declared.