Coronary risk variables in young asymptomatic smokers

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Background & objectives: Smoking plays a dominant role in premature atherosclerosis particularly among males in South Asian countries. It initiates and promotes atherosclerosis by altering cardiac haemodynamics, causing dyslipidaemia and producing oxidative damage. Not much information is available from our country. We therefore undertook this study to see the effect of smoking on electrocardiogram (ECG), blood pressure, lipids, apolipoprotein B level and free radical activity in young asymptomatic male smokers.

Methods: The study included 100 consecutive male subjects (50 smokers and 50 non smokers) aged 30-40 yr. Smoking profile, detailed cardiovascular assessment including ECG and lipid profile were evaluated in each subject.

Results: Of the 50 smokers, 22 (44%) had grade I hypertension as against 5 of 50 non smokers. Sinus tachycardia (10%) and P-pulmonale (8%) were the only notable ECG abnormalities. Dyslipidaemia was detected in 92 per cent smokers and 48 per cent non smokers (P<0.001). Total serum cholesterol, low density lipoprotein (LDL)-cholesterol, triglycerides and apolipoprotein B levels were significantly higher (P<0.001) in smokers compared to non smokers. LDL-cholesterol was >135 mg/dl in 94 per cent dyslipidaemic smokers. However, no significant difference was found in high density lipoprotein (HDL)-cholesterol. Smokers had significantly higher serum malondialdehyde levels (P<0.001) and low superoxide dismutase (P<0.001) compared to non smokers.

Interpretation & conclusion: Our data indicate that young asymptomatic male smokers tend to have hypertension, dyslipidaemia and increased production of free oxygen radicals, perhaps by attenuation of oxidative stress by cigarette smoking. This makes them prone for premature coronary artery disease. However, the findings need to be confirmed on a larger sample.

Key words  Apolipoprotein-B - dyslipidaemia - hypertension - oxidative stress - young asymptomatic smokers

Coronary artery disease (CAD) is one of the major health problems responsible for increasing mortality and morbidity in Indian subcontinent as well as in ethnic Indian communities all over the world. Its aetiopathogenesis is multifactorial. Smoking is considered to be the most important risk factor for CAD in young subjects. Most epidemiological data in single and cross-cultural populations have strongly linked tobacco smoking, hypertension, elevated total and low density lipoprotein (LDL) cholesterol to the subsequent development of CAD. It is also believed that modification of LDL increases its atherogenicity.
The free radicals alter the lipid metabolism and form oxidized and cytotoxic LDL, which is considerably more atherogenic than native LDL. Several clinical studies have recently focused on the strong correlation between levels of certain apolipoproteins particularly Apo B, and incidence and severity of CAD. However, there is not much information on young asymptomatic smokers in our country. It appears that oxidative stress consequence to smoking is one of the factors which promotes. We therefore studied the effect of smoking on changes in electrocardiogram (ECG), blood pressure (BP), serum lipids, Apo B and lipid peroxides to assess the coronary risk in young male asymptomatic individuals.

**Material & Methods**

**Study population and design:** The study was carried out in the Departments of Biochemistry and Medicine at University College of Medical Sciences and Guru Teg Bahadur Hospital, Delhi. A total of 100 consecutive male asymptomatic individuals (50 non-smokers and 50 smokers) in the age group 30-40 yr were selected from the volunteers who were invited to participate in this study through advertisements in the college and hospital notice boards and also through individual contacts during April 1999 to March 2000. History of smoking, duration and number of cigarettes/bidis smoked/day, height and weight were evaluated in each subject. Subjects smoking more than 5 cigarettes/bidis per day currently for more than six months were labelled as smokers in the present study. Smoking was defined as continuous use of bidi, cigarette and/or any form of tobacco for more than six months. Non smokers were those who never smoked.

Smokers were divided into the following categories as per criteria of Rastogi et al9: (i) *Mild smokers:* Subjects smoking 1-10 cigarettes or 1-15 bidis per day; (ii) *Moderate smokers:* Subjects smoking 11-20 cigarettes or 16-30 bidis per day; and (iii) *Heavy smokers:* Those who smoked 21 or more cigarettes or 31 bidis per day.

These subjects had no clinical evidence of CAD, had no past history of diabetes and/or hypertension (defined as systolic BP >140 mmHg; diastolic BP >90 mmHg). Hypertension was defined as per the JNC VII criterion10. Subjects with renal impairment, liver dysfunction, infection and alcohol intake were excluded from the study. Controls were age, weight and height matched nonalcoholic healthy men. Prior to participation, the purpose of the study was explained to all and their signed informed and written consent was obtained according to ethical principles of ICMR, New Delhi, India.

**Clinical studies:** A complete physical examination was carried out in each subject with particular emphasis on cardiovascular system. Dyslipidaemia was defined when any of the lipid fractions was deranged, [total serum cholesterol >200 mg/dl; high-density lipoprotein cholesterol (HDL-C) <35 mg/dl; low-density lipoprotein cholesterol (LDL-C) >135 mg/dl; serum triglycerides > 200 mg/dl]11. A 12 lead electrocardiogram was recorded in each subject. The ECGs were evaluated for any cardiac abnormality in terms of rate, frontal axis deviation, conduction defect, arrhythmia, chamber hypertrophy or any change suggestive of ischaemia.

**Experimental studies:** Blood samples (5 ml) were collected from all subjects in the fasting state (12 h overnight fast). Basic haematological parameters [total and differential leucocyte counts (TLC), (DLC) and haemoglobin] were done within 6 h after blood collection. Blood sugar (fasting and post-prandial) was estimated by glucose-oxidase method12. Total serum cholesterol13, HDL-C14 and triglycerides were estimated by enzymatic method15. LDL-cholesterol was calculated using Friedwald’s formula16. Atherogenic index was calculated from above values. Apolipoprotein B was measured by immunoturbidometric assay using kit (Randox Laboratories Ltd., UK)17.

Free radical production was measured by estimating malondialdehyde (MDA)18 and radical scavenging enzyme superoxide dismutase (SOD)19.

**Statistical analysis:** Demographic and clinical data from the two groups were compared and inter-group differences between the parameters were studied by using unpaired Student ‘t’ test with *P*<0.05 considered as significant.

**Results**

**Baseline characteristics of the subjects:** Among the 50 smokers, 31 (62%) belonged to moderate, 10 (20%)
mild and 9 (18%) heavy smoking category (Table I). There was no significant difference in the systolic and diastolic blood pressure between smokers and non-smokers. However, 22 of 50 (44%) smokers were found to have stage I hypertension as against 5 (11%) of non-smokers; 38 per cent of smokers and 44 per cent of non-smokers were prehypertensives [subjects with systolic blood pressure 120-139 mm/Hg and/or diastolic blood pressure 80-89 mm/Hg] (Ref.: The Seventh Report of Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure. *JAMA* 2003; 289: 2560-72). Interestingly, 4 (8%) smokers showed P-pulmonale. None of the subjects in either group had evidence of P-mitrale, right ventricular hypertrophy (RVH), left ventricular hypertrophy (LVH), right bundle branch block (RBBB), left bundle branch block (LBBB) or ST segment (ST) changes.

**Laboratory findings:** The mean value of serum total cholesterol was 227 ± 24.8 and 195 ± 25.5 mg/dl in smokers and non-smokers respectively. Eighty six per cent subjects in group I were having serum total cholesterol levels >200 mg/dl. Mean HDL-cholesterol (HDL-C) levels were 37.6 ± 6.6 and 40.1 ± 8.0 mg/dl in smokers and non-smokers respectively; 17 (34%) smokers and 5 (10%) non-smokers had serum HDL-C levels less than 35 mg/dl. Forty two (84%) smokers had serum LDL-C levels >135 mg/dl. Smokers group showed significantly (*P*<0.001) higher serum triglyceride levels (145 ± 60 mg/dl) as compared to non-smokers (111 ± 32 mg/dl). Mean values of serum apolipoprotein B were significantly (*P*<0.001) increased in smokers compared to non-smokers (Table II).

Serum lipid peroxides (MDA) levels were significantly higher (*P*<0.001) in smokers (2.62 ± 0.19 mmol/ml) compared to non-smokers (1.91 ± 0.21 mmol/ml), showing increased lipid peroxidation in smokers. However, mean values of erythrocyte superoxide dismutase (SOD), a scavenger enzyme for lipid peroxidation was significantly decreased (*P*<0.001) in smokers (941.7 ± 106 U/g Hb) compared to non-smokers (1452 ± 214 U/g Hb).

**Discussion**

The subjects included in this study were mostly from the middle or poor socio-economic strata and all of them belonged to eastern region of Delhi. Though there was no significant difference in the systolic and the diastolic BP levels, more number of smokers had higher systolic and diastolic blood pressure compared to non-smokers. High number of prehypertensives in the non smoker group is a matter of concern. This probably reflects the current status of increasing prevalence of hypertension in the community.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Smokers (Group I)</th>
<th>Non-smokers (Group II)</th>
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<tbody>
<tr>
<td>Age (yr)</td>
<td>33.7 ± 3.0</td>
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<tr>
<td>BMI (kg/m²)</td>
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<td>21.2 ± 2.0</td>
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<tr>
<td>Systolic BP (mm of Hg)</td>
<td>132.0 ± 13.6</td>
<td>128.5 ± 16.2</td>
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<tr>
<td>Diastolic BP (mm of Hg)</td>
<td>85.6 ± 5.2</td>
<td>83.3 ± 7.3</td>
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<td><strong>Smoking category no. (%)</strong></td>
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Values are mean ± SD

Table I. Baseline characteristics of smokers and non-smokers

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Eight per cent smokers showed changes of P-pulmonale on their ECGs. This might be due to development of corpulmonale subsequently producing right atrial hypertrophy as a result of chronic smoking. None of subjects in either group demonstrated any ventricular chamber hypertrophy, conduction defects or changes of ischaemia. This may be because of the inclusion of young subjects for the study while symptomatic subjects were excluded.

Our findings of elevated serum total cholesterol, LDL-C and triglycerides in the smokers were in concurrence with other workers\textsuperscript{20,21}. However in an earlier study no change was observed in cholesterol levels in smokers\textsuperscript{22}. Rastogi \textit{et al}\textsuperscript{6} reported significant decrease in the mean serum HDL-C levels in smokers compared to non smokers. This is in consonance to our observations wherein 17 (34\%) smokers compared to 5 (10.5\%) non smokers had serum HDL-C levels <35 mg/dl. Though the mean HDL-C levels were not significantly different in the two groups, more smokers were dyslipidaemic in terms of decreased HDL-C levels. Interestingly, increase in serum HDL-C levels have also been reported after cessation of smoking\textsuperscript{23,24}.

In terms of dyslipidaemia, 92 per cent smokers and 48 per cent non smokers had deranged lipid profile when all or any one of the criteria for dyslipidaemia was considered. Among the smokers, 84 per cent had LDL-C >135 mg/dl, signifying LDL-C as the most important lipid derangement consequent to smoking. Similar observations have been made by Freeman \textit{et al}\textsuperscript{25} who demonstrated a stronger association between smoking and the levels of triglycerides and LDL-C. The smokers had increased ratio of LDL/HDL. This obviously leads to increased risk of atherosclerosis and CAD. Smoking may influence the lipid levels by decreasing lipoprotein lipase activity, increased hepatic lipase and decreased lecithin cholesterol acyltransferase (LCAT) activity\textsuperscript{26}.

Apolipoprotein B, the major protein constituent of LDL, may provide more information on coronary heart risk than LDL-cholesterol alone\textsuperscript{27}. Avogaro \textit{et al}\textsuperscript{28} suggested that apolipoprotein B may be a better predictive factor than cholesterol and triglycerides. We found significantly higher apolipoprotein B levels in smokers compared to non smokers. Schaefer \textit{et al}\textsuperscript{27} have suggested that apo-B levels above 125 mg/dl were associated with increased risk for CAD. Framingham offspring study\textsuperscript{29} has also reported that apo B levels are associated with CAD in both men and women in spite of lack of a similar association between LDL-cholesterol and CAD in men.

Smoking is known to produce free oxygen radicals in our body\textsuperscript{30}. An excess of free oxygen radicals production due to lack of antioxidant, may increase the risk of CAD. In the present study lipid peroxide (MDA) levels were found significantly higher in smokers as compared to non smokers. Fabbri \textit{et al}\textsuperscript{31} reported increased MDA in CAD patients as compared to healthy controls. Yeolekar and Nargund\textsuperscript{32} postulated that hypertensive and smokers have increased oxidative stress.

Antioxidative activity was measured by estimating erythrocyte SOD in the present study. Erythrocyte SOD was found to be significantly decreased in smokers when compared to non smokers. Alam \textit{et al}\textsuperscript{33}

\begin{table}
\centering
\caption{Serum lipid profile and apolipoprotein-B levels in smokers and non smokers}
\begin{tabular}{lcc}
\hline
Variable & Smokers & Non smokers \\
\hline
Total serum cholesterol (mg/dl) & 227 ± 24.8* & 195 ± 25.5 \\
HDL-cholesterol (mg/dl) & 37.6 ± 6.6 & 40 ± 8.0 \\
LDL-cholesterol (mg/dl) & 161 ± 25* & 128 ± 22.7 \\
Serum triglycerides (mg/dl) & 145 ± 60* & 111 ± 32 \\
Serum apolipoprotein B & 121.2 ± 18.6* & 76.6 ± 12 \\
\hline
\end{tabular}
n=50 in each group
\end{table}

*\(P<0.001\) compared to non smokers
HDL, high density lipoprotein; LDL, low density lipoprotein
observed decreased SOD activity levels in patients with myocardial ischaemia compared to healthy subjects. Granger et al. demonstrated complete protection against ischaemic tissue injury following intravenous administration of SOD. It may therefore be concluded that decrease in levels of SOD in smokers indicates that either the scavenging system has been consumed during smoking or it is suppressed. The major limitation of this study was the small sample size, hence the findings cannot be generalized. Further studies need to be done in various parts of the country on a larger sample to reach to a valid conclusion.

As Twardella et al. found that smoking cessation by individuals after an acute coronary syndrome (ACS) or coronary revascularization could cut a patient risk of another cardiovascular disease (CVD) event by up to 20 per cent over the next year, cessation of smoking may be one of the most vital steps to save young male smokers from getting premature CAD.

References


